## 100 Keynote Address

Keynote Address - Thursday

**100.001** Why Are There So Few Effective Treatments for Autism – and Can Translational Neuroscience Help?. D. G. Murphy*, *Institute of Psychiatry, King's College London*

## 101 Infant Brain Development

*Discussant:* D. A. Fair *Oregon Health & Science University*

*Organizer:* J. R. Pruett *Washington University School of Medicine*

Autism spectrum disorder (ASD) is strongly suspected to involve altered developmental trajectories for structural and functional brain organization. Prospective infant sibling studies have brought increased focus on examinations of these potential changes in the first years of life, including prior to symptom expression. ASD researchers and providers need to be knowledgeable about basic aspects of infant brain development to be the most effective consumers of emerging scientific information about ASD. This panel will provide the non-neuroscientist and non-neuroimager with basic information about infant brain development and essential scientific methods used for interrogating it. Presentations will cover cellular processes, milestones of pre- and postnatal brain development, genetic and experiential effects on these processes, fundamentals of magnetic resonance imaging studies of the developing infant brain, developmental factors that influence trajectories for change in brain morphometry, and basic findings from brain imaging studies in infancy. Increased knowledge of infant brain development and the methods used for studies of brain changes in the first years of life will better enable ASD researchers and providers to assess emerging information about potential brain-based contributions to ASD in the first years of life.

**101.001** Overview of Early Brain Development. C. A. Nelson*, *Boston Children's Hospital*

Background:

In this presentation I will provide an overview of the major developmental milestones of pre- and postnatal brain development. I will begin with the assertion that the initial scaffolding of the brain is provided by various genes and gene networks working in unison, but that postnatally, much of development is dependent on experience. After a brief introduction to embryology, I will turn my attention to describing the stages of brain development, including the formation of the neural tube (Neurulation), the genesis of both neurons and glia, cell migration, cellular differentiation (including both the formation of processes, such as axons, as well as synapses), and myelination. Following this overview, I will turn my attention to the experience-dependent nature of brain development, and will introduce the concepts of experience-expectant development, experience-dependent development, and critical periods. I will conclude with a discussion of how errors in brain development may lead to the development of autism.

Objectives: N/A

Methods: N/A

Results: N/A

Conclusions: N/A

**101.002** Development of Human Cerebral Cortex in Health and Disease. D. C. Van Essen*, *Washington University School of Medicine*

Background:

Cerebral cortex is the dominant structure of the human brain, and abnormalities in cortical circuitry are implicated in autism as well as many other brain disorders. In order to interpret disease-related abnormalities, it is important to gain a deeper understanding of normal brain circuitry, its variability across individuals, and its pattern of development.

Much of human cortical development occurs prenatally. During the second trimester, cortical neurons are born and migrate to form a thin and smooth cortical sheet. During the third trimester, the cortex expands dramatically in surface area, becomes highly convoluted, and differentiates into a mosaic that contains hundreds of anatomically and functionally distinct cortical areas. Complex but highly specific long-distance connections are established between nearby and distant cortical areas during this period via axonal fiber bundles in the white matter that underlies the cortical sheet. Mechanical tension generated by these axons may contribute to cortical folding, by bringing strongly connected regions more closely together.

Premature birth can impede the normal maturation of brain structure and function, resulting in a wide range of childhood behavioral

and learning disorders, including autism. Magnetic resonance imaging (MRI) provides a powerful tool for studying brain structure and function in premature infants. Such approaches will hopefully lead to insights that help in diagnosing and treating the effects of abnormal brain maturation.

Healthy infants born at term have a brain that is only one-third its adult size. Many aspects of cortical maturation occur postnatally, including a three-fold expansion in cortical surface area that allows cortical circuits to be heavily shaped by postnatal experience. Interestingly, postnatal cortical expansion is regionally non-uniform, with the greatest expansion occurring in regions implicated in higher cognitive functions.

MRI-based methods for studying human brain structure, function, and connectivity have improved dramatically in recent years, including major advances driven by the Human Connectome Project (HCP). A consortium of HCP investigators led by Washington University, the University of Minnesota, and Oxford University is using these methods to study brain circuits in healthy adult twins and their non-twin siblings. Advanced analysis methods, including novel approaches to brain parcellation, are enabling characterization of functionally distinct parcels in individual subjects and in the overall population. Comparisons across individuals are beginning to reveal aspects of brain circuitry that are related to specific behavioral capacities. Data from the HCP are made freely available to the neuroscience community for extensive data mining via a user-friendly informatics platform. Insights gained using HCP-generated datasets and future application of such approaches to autism should accelerate progress in understanding, diagnosis, and treatment of this serious brain disorder.

Objectives: N/A

Methods: N/A

Results: N/A

Conclusions: N/A

**101.003** Imaging Infant Brain Development from Birth to 2 Years. J. H. Gilmore*, *University of North Carolina School of Medicine*

Background: The first years of life are the most dynamic and perhaps the most critical phase of postnatal brain development. Concurrent with the rapid pace of structural brain growth is an equally rapid development of a wide range of cognitive and motor functions. Abnormalities in early postnatal brain development have been implicated in neurodevelopmental disorders, including overgrowth of gray matter volumes and abnormal white matter development in autism. In spite of its importance for understanding normal brain development and the early origins of neurodevelopmental disorders, our knowledge of human brain development in this crucial time period is still not well developed. The Early Brain Development Study at UNC
focuses on early childhood developmental trajectories and their relationship to cognitive development in typically developing children, in twins, and in children at high risk for psychiatric disorders.

Objectives: To summarize early childhood brain development in the first 2 years of life.

Methods: Over 800 children have had structural, diffusion tensor, and resting state functional MRI scans at birth, with follow-up scans and cognitive assessments at ages 1, 2, 4 and 6 years. DNA has been collected on most children as well.

Results: There is rapid growth of overall brain size, driven mainly by gray matter development, attaining almost 85% of adult volume by age 2 years. Cortical thickness reaches 95% of adult values by age 2 years and surface area reaches 69%. There are marked regional differences in cortical gray matter growth, consistent with temporal patterns of sensory/motor and higher integrative function development. Most white matter tracts, including short cortico-cortical fibers, arise during prenatal brain development and are present at birth. There is rapid tract-specific maturation as reflected in diffusion tensor properties. Cortical gyrification and folding at birth is very similar to that observed in adults and we have found very little change in the first years of life. We have conducted a series of resting state fMRI studies in our cohort and found that most resting state networks including the default, attention control, visual, and sensorimotor networks are established by age two years.

Conclusions: The picture is emerging that overall cortical structure and "hard wiring" of the brain is well developed at birth. By age 2 years, the

structural and functional network stage is largely set for future learning, neuroplasticity, and "fine tuning" of major structural connections already in place. Thus, we believe that the first two years of life are critically important for establishing the infrastructure for future cognitive development, are likely a major critical or sensitive period for psychiatric disorders risk, and suggest that the window for effective interventions may need to be before the age of two years.

**101.004** MR Imaging of Brain Development. R. C. McKinstry*, *Washington University School of Medicine*

Background:

The human brain undergoes tremendous changes in size, shape and complexity over the first few years of life. On physical exam, we observe a change in the head shape and the head circumference, as well as the attainment of developmental milestones. Magnetic Resonance Imaging (MRI) is perfectly suited for characterization of the underlying structural changes in the brain that accompany the outward changes that parents and pediatrician observe. MRI does not use ionizing radiation so there is no risk of cancer, which is important in the pediatric population since they are more sensitive to ionizing radiation than adults.

MRI of the brain uses radiofrequency (RF) energy in the presence of magnetic fields to excite the protons in water and then capture the signal the is emitted when the excess energy dissipates. The process of energy dissipation is called relaxation. Two fundamental tissue relaxation constants govern this process: T1 and T2. Almost all MRI protocols produce images with either T1-weighting or T2-weighting. T1-weighted images are hyperintense (bright) when T1 relaxation occurs quickly. The key driver for T1 relaxation in the brain is lipid (fat). Brain lipid content is greatest in the myelin sheath that covers the axons. At birth, there is very little mature myelin and thus very little lipid. As the brain matures, the white matter myelinates, which changes contrast from dark to bright on T1-weighted images. T2-weighted image contrast, on the other hand, is governed predominately by the tissue water content. More water in the brain leads to brighter signal on T2-weighted images. Over the first few years of life, the brain dries out in general and the water content in the white matter drops substantially. The result is that white matter changes contrast from bright at birth to dark by age 2 on T2-weighted images. At first glance, one would say that brain image contrast reverses on T1- and T2-weighted images between birth and age 2.

By observing the signal changes on T1- and T2-weighted images, we can track the change in brain size, the decrease in brain water content and the increased complexity of the folding pattern that result from the maturational process. What is more, we can see regional changes in white matter myelination that follow a predictable pattern and time course over the first few years of life. Specifically, brain myelination proceeds from bottom to top, back to front, and inside out. The onset of the signal changes due to myelination is delayed for T2-weighted images relative to T1-weighted scans, which adds to the precision of our temporal estimates.

Objectives:

After attending this presentation, you should be able to describe how water and myelin content changes during brain development influence the MR image appearance. Armed with this knowledge, you will understand that the time course and regional variation of brain MRI signal is dictated by maturational changes. The final step in the process will be to use a systematic approach to determine the child's brain age using MRI.

Methods: N/A

Results: N/A

Conclusions: N/A

## 102 Adult Outcome

*Organizer:* M. R. Mailick *Waisman Center, University of Wisconsin-Madison*

**102.001** Transitioning Together: A Multi-Family Group Psychoeducation Program for Adolescents with ASD and their Parents. L. E. Smith*[1], M. R. Mailick[2] and J. Greenberg[3], (1)*University of Wisconsin-Madison*, (2)*Waisman Center, University of Wisconsin-Madison*, (3)*University of Wisconsin*

Background: Autism spectrum disorders (ASDs) are developmental disabilities characterized by difficulties in social communication and repetitive behaviors. ASD affects an estimated 1 in 88 children in the US. However, there are few programs available for children with ASD and their

families during the transition to adulthood. The paucity of evidenced-based programming during this period is especially concerning given that past research has shown adolescence to be a time of notably high stress.

Objectives: The present study aimed to evaluate *Transitioning Together,* a multi-family group psychoeducation intervention program for adolescents with ASD and their families.

Methods: For the present study, 30 families of adolescents with ASD (aged 14-17 years; M=15.98; SD=1.09) were drawn from an ongoing, randomized control study of the *Transitioning Together* program. Intelligence quotient scores for the adolescents ranged from 71 to 128 (M=102.07; SD=16.92) and 67% of adolescents were taking at least one medication. The majority of adolescents were White (90.6%) and male (70%). Over three quarters of parents had a college degree and most were working part or full time (75%). Families were randomly assigned to either an initial intervention (n=16) or waitlist control condition (n=14). The intervention involved individual 2 family joining sessions, 8 weekly parent and teen group sessions, and ongoing resources and referrals. Parent group sessions involved education on a variety of topics relevant to ASD as well as guided practice in problem-solving. The session topics included: (a) autism in adulthood, (b) transition planning, (c) problem-solving, (d) structuring the family environment, (e) risks for adult independence, (f) community involvement, (g) parental health, and (h) legal issues. The adolescent social group involved learning activities and games on topics such as sharing interests, goal setting, problem solving, and social planning. Parents and adolescents completed interviews and questionnaires at pre- and post-intervention as well as completed surveys during each weekly session.

Results: There were significant improvements in parent attitudes about their teens from pre- to post-intervention for initial intervention families compared to controls. There were also trends for improvements in parental depressive symptoms, expressed emotion, and family empowerment, for the intervention group relative to the control group. Data collection and intervention groups are ongoing (est. total n~50), which will increase the statistical power for analyses. Parents and teens reported strong satisfaction with the program (nearly 100% retention) and adolescent engagement during group interactions increased over the course of the 8 sessions. In response to open-ended questions, adolescents self-reported learning about planning, eye contact, how to cope with stressful situations, and general (often idiosyncratic) facts. Parents most frequently indicated learning about legal issues, vocational rehabilitation services, and community activities. Other themes that emerged from parent exit interviews included the value of connecting with other families, not feeling alone, and hope.

Conclusions: These findings highlight the value of the *Transitioning Together* program for families of teens with ASD, with benefits for parental well-being and the family climate. Findings also suggest that teens value the opportunity to interact and learn with peers on the spectrum.

**102.002** Psychiatric and Medical Conditions Among Adults with ASD.

L. A. Croen*, O. Zerbo, Y. Qian and M. L. Massolo, *Kaiser Permanente Northern California*

Background: Children with autism spectrum disorders (ASD) have been shown to have a higher burden of medical and psychiatric comorbidities and increased utilization of health care services compared to the general pediatric population. However, very little is known about the general health status among the adult ASD population. Given that increasing numbers of children are entering adulthood each year with an ASD diagnosis, an understanding of this issue is critical for resource planning and the development of effective strategies for health care delivery to adults with ASD.

Objectives: To describe the frequency of psychiatric and medical conditions among a large, diverse, insured population of adults with ASD in the US.

Methods: The study population was drawn from the adult membership (≥ 18 years) of Kaiser Permanente Northern California (KPNC) (~2.5 million) enrolled in the health plan for at least 9 months each year from 2008-2012. Physician documented diagnoses routinely captured in KPNC electronic medical records were utilized for all analyses. ASD cases (N=2,108) were adults with at least one ASD diagnosis (ICD-9-CM 299.0-299.8) recorded by December 2012. A control group of adults without any ASD diagnoses

(N=21,080) were sampled at a 10:1 ratio and frequency matched to cases on total length of KPNC membership, sex, and age. We compared the prevalence of psychiatric, behavioral, and medical conditions overall and by sex, age group, and race/ethnicity between cases and controls.

Results: Adults with ASD had significantly increased rates of depression (38% vs. 17%), anxiety (39% vs. 18%), bipolar disorder (8% vs. 1%), and suicide attempts (1.6% vs. 0.3%), and prevalence differences between cases and controls increased with age. Among women, rates of alcohol and chemical dependency were 2-fold higher in ASD cases than controls. Nearly all medical conditions were significantly more common in adults with ASD than controls: diabetes (6% vs. 4%), gastrointestinal disorders (47% vs. 38%), epilepsy (12% vs. 1%), sleep disorders (19% vs. 10%), dyslipidemia (26% vs. 18%), hypertension (27% vs. 19%), and obesity (27% vs. 16%). Among women, asthma, allergy and autoimmune disorders were present 20%-30% more often in adults with ASD than controls. Rarer conditions, such as eating disorders, mechanical falls, vision and hearing impairments, osteoporosis, and chronic heart failure were also significantly more common among adults with ASD than controls. Rate differences between cases and controls were variable across race/ethnic groups, especially for diabetes and epilepsy. Of note, adults with ASD were significantly less likely to use alcohol (23% vs. 53%) or smoke (16% vs. 30%). Finally, the rate of cancer was similar between ASD cases and controls (2.7% vs. 2.6%).

Conclusions: Adults with ASD have a significant burden of major psychiatric and medical conditions. Their underlying impairments in social communication and increased sensory sensitivities likely impede the delivery of preventive health care. Improved strategies for delivering the most appropriate and effective health care are needed for this growing population.

**102.003** A Quantitative and Qualitative Study of Twenty Autistic Individuals Over 50 Years of Age. J. Piven*[1], P. Dilworth-Anderson[2] and M. Parlier[3], (1)*University of North Carolina at Chapel Hill*, (2)*Institute of Aging*, (3)*University of North Carolina*

**Background**: Originally described as a disorder of childhood, evidence now demonstrates the lifelong nature of autism spectrum disorder (ASD). Despite the increase of the general population over age 65, older adults with ASD remain a scarcely explored subpopulation. With the aging of the ASD population in western countries, increasing rate of diagnosis of ASD and burgeoning use of services by persons with ASD, the need to learn more about aging and autism is a high priority. In this study we cast a broad net by conducting both a qualitative and quantitative descriptive study, in order to identify areas of focus for future studies of this population.

**Objectives**: 1) Explore the issue of ascertainment bias in finding older individuals with ASD, as this will undoubtedly influence the interpretation of any future studies. (2) Examine the life stories, current and retrospective behavior, co-occuring medical and psychiatric problems, life circumstances and quality of life of older adults with ASD.

**Methods**: We surveyed over a wide range of individuals, families and agencies including - hospitals, statewide advocacy organizations, specialty clinics, state residential facilities, general medical practices and a statewide autism registry, to identify 20 adults with ASD over 50 years of age. Informants and subjects were assessed on measures of autistic behavior; cognitive ability; medical/neurological and psychiatric problems; level of function; family and community supports and services; and quality of life.

**Results**: Twenty individuals over 50 years of age were identified from mailings to over 14,000 households and agencies in North Carolina. Bias of ascertainment was apparent and linked to the ascertainment source e.g., severe intellectual impairment characterized those ascertained through residential facilities; medical problems were common in those ascertained through general hospital records. Major themes identified included (a) the impact of wide variation in lifelong family support; (b) early difficulties obtaining accurate diagnosis with a resultant negative impact; (c) high rates of treated psychiatric and behavioral problems; (d) difficulty finding appropriate residential environments; and (e) victimization. More detailed quantitative analyses will be presented.

**Conclusions**: The results of this descriptive survey suggest that future studies of this population will be affected by a significant bias of

ascertainment as well as the likelihood that many older individuals with ASD, in the community, have been misdiagnosed with something other than ASD. The high rate of significant behavioral/psychiatric problems suggest the urgent need for research on the nature and treatment of behavior problems in this rapidly expanding population of older adults with ASD, as well as the importance of developing policies to expand our capacity to care for these individuals.

**102.004** Academic and Personality Profiles of Higher Education Students with ASD. W. Tops*[1], D. Baeyens[2] and I. Noens[3], (1)*LAuRes*, (2)*Thomas More*, (3)*KU Leuven*

Background: An increasing number of students with ASD enter higher education, most likely due to better assessment, guidance and remediation in primary and secondary education. There is a lack of effective educational support services for adolescents with ASD to make smooth transition from secondary to higher education, jeopardizing the academic outcome of this group.

Objectives: Better insight in the specific difficulties and strengths and weaknesses of students with ASD is needed, especially in tertiary education. The first purpose of this study was to focus on the academic and personality profiles of students with ASD starting in their first year of higher education. Second we wanted to develop a theoretical framework for the guidance of students with ASD in higher education.

Methods: Twenty-seven first bachelor students with ASD and 52 students with no neurological or functional deficiencies participated in this study. The students with ASD were diagnosed prior to this study in a multidisciplinary context according to DSM-IV criteria but all had (sub)clinical scores on the SRS-A at the time of participation. A wide range of academically relevant skills, such as IQ, vocabulary, memory (KAIT), reading and writing (GL&SCHR) were administered. Next, we also took personality (NEO-PI-R) and study strategies inventories (LASSI) to get better insights in the study skills (metacognitive knowledge) and personality profile of students with ASD. ASD and control groups were compared using Hedges' g effect sizes.

Results: Students with ASD scored lower on reading and writing skills ($-0.4 < d < -1$) but they were as good as the control student on text comprehension. As for the study strategies inventory, students with ASD had poorer study techniques ($d = -0.8$) and test strategies ($d = -0.4$) than their peers without ASD. However, first bachelor students with ASD obtained significantly higher scores on a fluid intelligence scale than control students ($d = 0.4$). Short and long term memory skills were also higher in the ASD group than in the control group ($0.2 < d < 0.6$). Finally, students with ASD had a specific personality profile: students with ASD obtained lower scores for extraversion ($d = -1.2$), openness (-0.6), and agreeableness (-0.6) than control students. There was no difference for neuroticism (0.05) and conscientiousness ($d = 0.2$).

Conclusions: Results show particular strengths and weaknesses in students with ASD. With these strengths some students can hypothetically compensate for ADS-specific impairments (EF, ToM, CC). We pointed out specific challenges for students with ASD and educational support services that can hopefully lead to better guidelines en regulations for these students. Implications for psycho-education and special arrangements in higher education for students with ASD are also discussed.

**102.005** Self Reports of ASD Symptomatology, Cognitive Failures, & Quality of Life in Adults (19-79 years) with ASD: A Cross Sectional Study. H. M. Geurts*[1] and A. G. Lever[2], (1)*University of Amsterdam*, (2)*Dutch Autism & ADHD research center, Brain & Cognition, University of Amsterdam*

**Background**: There are only a handful of studies focusing on aging in ASD, but findings from studies including people with ASD in young and late adulthood suggest that, for example, some ASD symptoms abate while others remain stable or even increase. Moreover, with healthy aging we know that cognitive processes, but sometimes also quality of life (QoL) declines. Whether this is also the case for people with ASD is unknown.

**Objectives**: To determine by means of self-report questionnaires the relationship between age and ASD symptomatology, cognitive failures, and QoL in adults and the elderly with ASD.

**Methods**: People aged 19 to 79 years (IQ>80) with a clinical diagnosis of ASD and controls without an ASD diagnosis filled out a series of self report measures. We administrated the Autism Spectrum Quotient (AQ; N ASD=233; N Controls=125) to measure ASD symptomatology,

the quality of life questionnaire from the world health organization (abbreviated WHOQOL; N ASD=230; N Controls=124) to determine the experienced QoL, and the cognitive failure questionnaire (CFQ; N ASD=111; N Controls=91) to explore whether people with ASD experience more cognitive daily life challenges than people without ASD. We ran regression analyses to explore the role of age.

**Results**: Group comparisons revealed that adults and elderly with ASD experience lower QoL and more cognitive failures as compared to controls. Regression analyses showed that in addition to the group effect neither age (linear or quadratic) nor the interaction of age with group did explain extra variance. While there were marginally significant interactions between age and group for most questionnaire scores, this was only significant ($p$<.001) for the QoL physical health scale. Separate exploratory analysis for the two groups revealed that with increasing age people with ASD report an increase on the physical health QoL scale (i.e., improvement), while in the control group there seem to be no relationship between age and this QoL scale score. In both groups an increase in the environment QoL scale score with increasing age was observed. These results are preliminary as data collection will be finished in April 2014. As the data are a part of an ongoing project (funded by NWO-MagW) in which we also directly test comorbidity and cognition, we will directly test whether the experienced cognitive failures will relate to actual cognitive performance.

**Conclusions**: In the current study we did not find evidence for the idea that ASD symptoms decrease with increasing age. Moreover, even though people with ASD experience more cognitive difficulties as compared to controls, this was not differentially related to age. Age does seem to have a different effect on experienced QoL in people with ASD and controls and, according to people with ASD themselves, QoL is relatively low. Hence, it is of importance that there is sufficient professional and societal support for elderly people with ASD.

**102.006** Nonverbal IQ in Young Adults with Autism Spectrum Disorder: Correspondence with Scores from Early Childhood.

S. L. Bishop*[1], A. Thurm[2] and C. Farmer[3], (1)*Center for Autism and the Developing Brain, Weill Cornell Medical College*, (2)*National Institutes of Health - National Institute of Mental Health*, (3)*NIH*

Background: IQ has been studied as an important factor in predicting both current and future functioning in children with autism spectrum disorder (ASD). However, relatively little is known about longitudinal measurement and stability of IQ, particularly in children who span the full range of cognitive ability.

Objectives: To assess the stability of nonverbal IQ scores in a cognitively heterogeneous sample of individuals with ASD from toddlerhood to young adulthood.

Methods: A sample of 84 children diagnosed with ASD at age 2 years was tested again at age 3 and then followed through age 18. At each assessment, participants were administered developmentally-appropriate tests to obtain estimates of cognitive functioning either through standard IQ scores, if possible, or ratio-derived developmental quotients (DQs).

Results: Nonverbal IQ/DQ scores generally declined from 2 to 18 for the majority of individuals with ASD in the sample. While age 2 scores were predictive ($R^2$=.44), age 3 scores were slightly more predictive ($R^2$=.55). However, at both ages, relationships were generally stronger for individuals with lower nonverbal IQ/DQ. At age 2, $R^2$ = 0.35 for children with NVIQ/DQ < 70, while $R^2$ = 0.08 for children with NVIQ/DQ ≥70. At age 3, $R^2$ = 0.26 for children with NVIQ/DQ < 70, and $R^2$ = 0.17 for children with NVIQ/DQ ≥70. Broad score divisions (e.g., IQ/DQ over vs. under 70) showed relatively high stability, whereas narrower DSM-IV-based ability ranges (e.g., Borderline, Mild MR, etc.) were much less stable over time. At age 2, children were distributed as follows: Average (NVIQ/DQ ≥ 85, $n$ = 17), Borderline (NVIQ/DQ ≥ 70, $n$ = 26), and the remainder ($n$ = 41) fell into the ID range. Twenty-one were in the moderate to profound category (NVIQ/DQ< 50). At age 18, when 67% of the sample required use of a test outside of its standardized age range, the number of participants with NVIQ/DQ < 50 jumped to 45, while the Average ($n$ = 21) and Borderline ($n$ = 9) groups declined. Use of Vineland-II Daily Living Skills scores in place of nonverbal IQ/DQ scores at the age 18 time point did not improve the predictive validity of age 2 scores ($R^2$=.41).

Conclusions: These findings indicate that most children with ASD who exhibit significant

nonverbal cognitive "delays" as young children score in the range of intellectual disability as adults. On the other hand, the majority of individuals with nonverbal IQ scores in the average range or above by age 3 tended to continue to score in the average range or above at age 18. Particularly within the lower ranges of ability, this study indicates that "absolute" nonverbal IQ scores of individuals with ASD decline from age 2 to 18. However, limitations of available and appropriate tests may be significant factors in this decline, as well as growth in verbal skills during this time period. Clinicians and researchers should use caution when making comparisons based on absolute scores or specific ability ranges within or across individuals with ASD of different ages.

**102.007** Can Self-Report Questionnaires Screen for Autism in Adults? Comparison with 'Gold Standard' Diagnostic Assessments. K. L. Ashwood*, N. Gillan, J. Horder, F. S. McEwen, E. L. Woodhouse, H. L. Hayward, J. Findon, H. Eklund, D. Spain, C. E. Wilson, C. M. Murphy, D. Robertson, K. F. Glaser, P. Asherson and D. G. Murphy, *Institute of Psychiatry, King's College London*

**Background:** The prevalence of autism spectrum disorders (ASDs) is increasing. This has resulted in a growth in demand on clinical services, with more people referred for diagnostic assessment. Diagnosing ASD is expensive and time consuming, so there is a need for reliable, cost-effective screening instruments. The UK National Institute for Health and Care Excellence (NICE) has recently recommended using the Autism-Spectrum Quotient-10 item (AQ10) self-report questionnaire as a rapid screening tool for ASD in adults. However, while the AQ10 has been shown to discriminate between already-diagnosed ASD populations and healthy control groups, its performance as a predictor of ASD within real-world clinical populations has not been investigated.

**Objectives:** Our goal was to determine whether the AQ10 is able to predict ASD caseness in adult clinical settings. We also assessed the original, longer version of the AQ questionnaire, the AQ50, which has also been used as a screening tool.

**Methods:** 730 participants (548 males, 182 females, mean age 31.2) presenting to outpatient specialist services (N=620), inpatient psychiatric units (N=44) and primary care settings (N=66) completed the AQ. Participants were assessed for ASD using so called 'gold standard' instruments, the Autism Diagnostic Interview Revised (ADI-R) and the Adult Diagnostic Observation Schedule Generic (ADOS-G). The AQ10 and AQ50 were evaluated as predictors of meeting standard criteria for ASD caseness on i) the ADI-R and ii) the ADOS-G. We first calculated sensitivity, specificity and Youden's J (a measure of accuracy) of the AQ10 and AQ50 as dichotomous predictors, using recommended cut-offs. Secondly, Receiver Operating Characteristic (ROC) curve analysis was used to determine optimal cut-off scores.

**Results:** The AQ10 and AQ50 demonstrated poor informative power across all three patient samples and all comparison measures (Youden's J= 0-0.24) with higher sensitivity (0.33-0.87) than specificity (0.18-0.63). ROC curve analysis revealed that the ability of the questionnaires to predict ADI-R and ADOS-G caseness was in most cases statistically significant (AQ50: $p=0.025$, $p=0.001$ respectively; AQ10: $p=0.089$, $p<0.001$ respectively), but modest (area under curve, AUC 0.55-0.61, where 0.5 is chance). Furthermore, optimal performance was seen with higher cut-offs than those currently recommended (maximum Youden's J at AQ50: 36-37 and AQ10: 8).

**Conclusions:** For the first time, we have shown that scores on the AQ10 and AQ50 self-report scales predict caseness in an adult real-world clinical population. However, both screeners performed only slightly better than chance. Increasing the cut-off score above the recommended values improves psychometric properties, yet, this still only provides modest performance. Further work is needed to validate the AQ10 and/or AQ50 as clinical screening tools.

**102.008** Sleep Quality and Daytime Functioning in Adolescents and Young Adults with Autism Spectrum Disorders. J. N. Phung* and W. A. Goldberg, *University of California, Irvine*

Background: Children with Autism Spectrum Disorders (ASD) experience an increased prevalence of sleep problems relative to their typically developing peers. Recent research has identified that approximately 66% of children with ASD experience at least moderately severe sleep problems (Souders et al., 2009). Sleep problems, such as difficulty falling asleep and frequent and prolonged night wakings, are among the first

reported parental concerns to healthcare professionals among children later diagnosed with ASD (Guinchat et al., 2012). Children with ASD with problematic sleep demonstrate greater impairment in cognitive and behavioral domains compared to children with ASD without problematic sleep (Goldman et al., 2011). Siblings' and parents' sleep is also disrupted by the autistic child with sleep problems (Chou et al., 2012; Lopez-Wagner et al., 2008). Sleep problems in childhood may continue to persist into adolescence and adulthood, which may lead to further disturbances in individual functioning and family relationships.

Objectives: The objective of the current study was to examine how sleep quality and sleep architecture in individuals with ASD are related to psychological well-being, daytime functioning at school/work, and family relationships.

Methods: A well-characterized sample of adolescents and young adults with ASD and one of their parents were enrolled to participate. Target participants were first screened for eligibility using the Autism Diagnostic Observation Schedule (ADOS-2; Lord et al., 2000). Next, home visits were scheduled. During the first part of the visit, adolescents/young adults used pre-programmed iPads to report on sleep duration, sleep quality, psychological well-being, family relationships, and daytime functioning at school/work. Parents/caregivers also completed measures on an iPad. In the latter part of the visit, participants were instructed in the use of pre-programmed Smart Phones. The phone "apps" kept logs of participants' sleep quality for the next 7 nights and recorded well-being and relationship issues. Participants were also instructed to use a MicroMini Motionlogger actigraph, which collected objective sleep data to supplement subjective Smart Phone reports. A week later, the research team returned to the home to pick up the actigraph and phone.

Results: Preliminary results suggest significant associations between disrupted sleep, daytime sleepiness, and individual and family functioning. For example, adolescents who obtained more uninterrupted sleep during the night reported feeling more alert during the day compared to those who obtained less nighttime sleep. Furthermore, adolescents who had lower sleep efficiency also demonstrated poorer daily functioning at school, such as falling asleep during class. More nocturnal wakefulness was also associated with adolescent report of negative interactions with the participating parent, including higher perceived criticism. In sum, these data suggest that poor sleep quality is related to negative outcomes in individual and family well-being. Data on the full sample will be ready for presentation at IMFAR.

Conclusions: Early results confirm the utility of objective and subjective methods of collecting data on sleep quality. Quality of nighttime sleep relates to the functioning of adolescents with ASD and their parents. Understanding these associations can be used to advance the quality of life for families with ASD through sleep interventions and clinical implications.

## 103 Brain Function and Structure I

*Organizer:* D. G. Murphy *Institute of Psychiatry, King's College London*

**103.001** Mapping White Matter Development in Children and Adolescents with Autism. A. Shahidiani*[1], V. D'Almeida[2], L. Van-Hemert[2], N. Gillan[2], C. Ecker[2], C. M. Murphy[2], D. G. Murphy[2], S. C. Williams[1] and S. C. Deoni[3], (1)*Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry, King's College London*, (3)*School of Engineering, Brown University*

**Background:** Imaging studies of white matter (WM) volume (morphometry) and microstructure (predominantly assessed via diffusion tensor (DT)-MRI) throughout infancy, childhood and adolescence have shown consistent differences in regional WM development and architecture. Temporally coincident with the first reports of autistic symptoms and early micro-structural differences, is the process of myelination.

**Objectives:** To-date, no direct study of myelin development across childhood or adolescence in ASD has been performed. We sought to fill this knowledge gap, performing a cross-sectional study of myelin content in this age group.

**Methods:** 47 ASD males (5-17 years; 11.8±3.1), diagnosed according to the *International Statistical Classification of Diseases, 10th Revision*(ICD-10), confirmed using Autism Diagnostic Interview-Revised (ADI-R), and Autism Diagnostic Observation Schedule (ADOS), and 40 age and IQ-matched typically developing (TD) males (7-17 years;12.3±2.8) of IQ>70 were

recruited. A measure of myelin content, myelin water fraction (MWF), was acquired using the multi-component relaxometry technique mcDESPOT, which derives MWF estimates by fitting a three-pool model to a combination of T1-weighted SPGR and T2/T1-weighted balanced SSFP imaging data, with additional correction for B0 and B1 inhomogeneities.

After voxel-wise calculation of MWF maps and non-linear co-registration to a common template, mean myelin development trajectories were compared between ASD and TD groups in 12 predetermined WM pathways; as well as voxel-wise comparisons of WM. Developmental slopes for the 12 pathways were estimated using a wild bootstrap approach with residual re-sampling and then compared using an unpaired two-tailed t-test.

To investigate associations between MWF values and symptom measures in the ASD group, correlation analysis was performed on a voxel-wise level between the MWF values and ADOS and ADI-R sub-scores. Significance was defined as $p<0.05$, cluster corrected for multiple comparisons.

**Results:** The ASD group displayed lower absolute MWF values at 6 years, followed by an accelerated developmental trajectory leading to overall increased MWF by 17 years. The 'crossover' point at which ASD children went from reduced to increased MWF relative to controls was observed consistently between 12-13years across the majority of tracts.

MWF values differed significantly in; the body, genu and splenium of the corpus callosum; fornix; bilateral internal capsule; anterior thalamic radiations; bilateral uncinate and left inferior longitudinal fasciculus. Voxel-wise comparisons confirmed these results and also implicated the, bilateral corticospinal tracts; forceps; cingulum; inferior fronto-occipital fasciculus; portions of the superior longitudinal fasciculus; and cerebellum. Significant negative correlations were seen between MWF values and ADI-R sub-scores though no significant correlations were identified between myelin content and ADOS measures.

**Conclusions:** In this first cross-sectional analysis of myelin development through childhood and adolescence, we found that children with ASD had a significantly greater myelin development rate compared with TD children in brain regions previously implicated in ASD. Our findings argue for more statistically powerful longitudinal studies of myelin development that span development from infancy through to early adulthood to complete the picture of myelin development in typical development and ASD.

**103.002** Multiple Oxytocin Receptor Gene (OXTR) Loci Coalesce to Impact Structural Connectivity in Children with Autism.

L. M. Hernandez*[1], J. D. Rudie[2], D. Beck-Pancer[1], D. H. Geschwind[1], S. Y. Bookheimer[1] and M. Dapretto[1], (1)*UCLA*, (2)*Ahmanson-Lovelace Brain Mapping Center, UCLA*

**Background:** Recent neuroimaging-genetics research suggests that common single nucleotide polymorphisms (SNPs) associated with increased risk for Autism Spectrum Disorder (ASD) diagnosis may predispose to ASD through their effects on brain connectivity (e.g., Rudie, 2012). Given that social deficits are a core feature of ASD, here we examined a gene linked to increased risk for ASD diagnosis, as well as social and affiliative behavior across species: the oxytocin receptor gene (OXTR). Genetics research has identified an association between increased risk for ASD and multiple OXTR SNPs (e.g., Wu, 2005; Jacob, 2007). Findings of multiple risk loci on the OXTR gene in ASD support a "multiple-hits" model of autism etiology in which individuals who carry greater numbers of risk alleles are at increased likelihood for presenting more atypical neural endophenotypes (Huguet, 2013).

**Objectives**: Here, we investigated how the presence of risk alleles across multiple OXTR SNP loci may coalesce to produce an additive effect on structural connectivity in typically developing children (TD) and children with ASD. We explored two models: 1. How multiple ASD-associated OXTR SNPs impact whole brain structural connectivity. 2. How multiple social behavior-associated OXTR SNPs impact whole brain structural connectivity.

**Methods:** DNA was extracted from saliva samples and genotyped for six ASD-associated OXTR SNPs (rs53576, rs1042778, rs2254298, rs237884, rs237895, rs7632287) and two social behavior-associated SNPs (rs237887, rs2268491). Sixty-two children (31ASD, 31TD) underwent 32-direction diffusion tensor imaging (DTI). Data was

analyzed using Tract Based Spatial Statistics (Smith, 2006) to investigate voxelwise white matter (WM) fractional anisotropy (FA; a measure of fiber integrity). Total number of risk alleles across SNPs was used to create an aggregate risk score for each subject and entered as a covariate to assess whether the relationship between FA and aggregate risk score differs between the two diagnostic groups (TD and ASD).

**Results:** Greater numbers of ASD-associated OXTR SNPs were associated with decreased FA in the ASD group in the bilateral body of the corpus callosum, left inferior longitudinal fasciculus, left inferior fronto-occipital fasciculus, left external capsule, left internal capsule, and left uncinate fasciculus ($p<0.05$, corrected). A significant interaction was present such that greater aggregate risk sores were associated with reduced FA in ASD participants above the effect observed in TD participants ($p<0.05$, uncorrected). When additional OXTR SNPs related to social behavior were added to the aggregate risk score, greater numbers of risk alleles were associated with decreased FA in the body of the corpus callosum bilaterally and left superior longitudinal fasciculus for the combined TD and ASD group ($p<0.05$, corrected), as well as for the TD and ASD groups separately ($p<0.05$, uncorrected).

**Conclusions:** Our results indicate that aggregate OXTR risk is associated with reduced WM fiber integrity in long-range fiber tracts connecting anterior and posterior brain regions in TD and ASD children and reduced WM integrity in tracts connecting subcortical and limbic structures (in ASD participants only). These data suggest that OXTR SNPs influence patterns of structural brain connectivity, which may be modulated by diagnostic status and vary as a function of aggregate risk status.

**103.003** Altered Amygdala Nuclei Projections in Young Adults with Autism Spectrum Disorder. C. R. Gibbard*, J. Ren, D. H. Skuse, J. D. Clayden and C. A. Clark, *UCL Institute of Child Health*

Background:

Structural magnetic resonance imaging (MRI) studies of autism spectrum disorder (ASD) report both amygdala enlargement and reduction in ASD, whilst functional MRI studies have shown reduced amygdala activation in response to social cues. The amygdala comprises several nuclei, each with specific white matter (WM) connections. Recent diffusion tensor imaging studies segmented the healthy adult amygdala into subregions *in* vivo using WM connectivity-based parcellation schemes.

Objectives:

To investigate amygdala sub-structure in ASD using *in vivo* WM connectivity information.

Methods:

25 high-functioning ASD (mean age: 24.7yr) and 26 neurotypical (mean age:23.2yr) subjects underwent whole-brain $T_1$-weighted ($1mm^3$) and diffusion-weighted ($2.5mm^3$; 60 directions $b=1000s/mm^2$; 3 $b=0$) MRI on a 1.5T Siemens Avanto scanner. Diffusion data were pre-processed using FSL. Amygdala and whole brain regions of interest were delineated using the FSL tools FIRST and SIENAX. Cortical regions were generated using FreeSurfer. Cortical targets were grouped into frontal, parietal, occipital, and temporal lobes, and the insula using FSL utilities. All regions of interest were registered to diffusion space using the FSL tools FLIRT and FNIRT. TractoR was used to seed probabilistic tractography from each amygdala voxel to the five cortical targets. An iterative 'winner takes all' process was used to assign a winning target to each voxel. Voxels maximally connected to the same target were considered a cluster. WM tract fractional anisotropy (FA) and mean diffusivity (MD) were measured. Group comparisons were made using linear regression. Correlations with the self-reported autism quotient (AQ), a measure of ASD severity, were made within the ASD group using partial Spearman correlation. Age, gender and full-scale IQ were covariates.

Results:

Right amygdala volume, normalized as a percentage of whole brain volume, was significantly elevated in ASD compared to neurotypical controls ($t=2.01$; $p=0.05$). There was no significant group difference in left amygdala volume. MD was significantly elevated in the ASD group in WM tracts connecting the left amygdala with the left cortex ($t=2.53$; $p=0.02$) and the right amygdala with the right cortex ($t=2.95$; $p=0.005$). The 'winner takes all' algorithm resulted in clusters of amygdala voxels

connecting to all cortical targets, aside from the occipital lobe. MD of WM tracts connecting the left amygdala-left temporal lobe cluster was significantly higher in ASD (t=2.11; p=0.04). Within the ASD group, negative correlations were observed between AQ score and FA of WM tracts connecting the left (rho=-0.51; p=0.009) and right (rho=-0.51; p=0.009) amygdala-temporal lobe clusters (both survive FDR-correction).

Conclusions:

We report alterations in amygdala volume and structural connectivity in young adults with ASD. These findings were particularly apparent for the right amygdala, indicating that it is more involved in, or affected by, ASD pathology than its counterpart in the left hemisphere. Our structural parcellation results demonstrate that local connections between the amygdala and the temporal lobe are particularly affected in ASD, with greater aberrations in these local connections strongly related to increased ASD severity. This is the first study to parcellate the ASD amygdala based on its WM connections; our findings indicate that amygdala sub-regions have distinct involvement in ASD impairment.

**103.004** Lateralization of Brain Networks and Clinical Severity in Toddlers with Autism Spectrum Disorder: A Diffusion MRI Study. E. Conti*[1], S. Calderoni[1], A. Gaglianese[1], K. Pannek[2], S. Mazzotti[1], D. Scelfo[1] and A. Guzzetta[1], (1)*Stella Maris Institute*, (2)*University of Queensland Centre for Clinical Research*

Background: Recent diffusion imaging and tractography studies in adolescents and young adults with ASD have reported a loss or an inversion of the left–right asymmetry in regions crucial for socio-communicative skills, including the Cingulate, Arcuate Fasciculus, Uncinate Fasciculus, Superior Temporal Gyrus and neural circuits involving the fusiform. Few studies explored atypical lateralization in younger children and its correlation with clinical severity of ASD.

Objectives: We studied a group of children younger than 36 months with a first clinical diagnosis of ASD. Our aim was to measure the laterality indexes of white matter pathways on brain diffusion MRI, in order to determine their correlation with clinical severity of ASD, as assessed by ADOS-G.

Methods: As part of an ongoing prospective project, started on January 2012, we selected all children referred to our tertiary care centre for social-communication impairment. Subjects were included in the present study if they i) received a clinical diagnosis of ASD based on DSM IV, ii) were aged 36 months or less and iii) had no neurometabolic or genetic disorders. Twenty-four subjects fulfilled our inclusion criteria. Four patients were excluded due to incomplete MRI assessment. The final cohort consisted of 20 subjects (15 males; mean age 28 +/- 4.7 months; age range 20-36 months).

Brain MRI was performed on a GE 1.5 T scanner. High angular resolution diffusion imaging (HARDI) scans were acquired using either 31 or 65 diffusion weighted images (b value = 1000 s x mm^-2). Image post-processing consisted of cortical parcellation (FreeSurfer software) on high resolution T1 image and whole brain fibre tracking by constrained spherical deconvolution (MRtrix software). Data from cortical parcellation were combined with tractography to obtain a connection matrix, and within each pair of connected areas, diffusion indexes ($D_i$) were obtained including mean fractional anisotropy (FA), number of streamlines (NUM) and tract volumes (VOL). A laterality index was generated for each connected pairs according to the following formula: (right $D_i$ – left $D_i$ / right $D_i$ + left $D_i$).

We correlated laterality indexes from each pair of connected areas with the ADOS-G total score using Pearson's linear correlation coefficient. Correlation values were corrected for multiple comparisons based on a false discovery rate of 10%.

Results: Laterality indexes of FA were significantly correlated with ADOS total scores only in two intra-frontal connected areas (correlation was positive in 1 case and negative in the other). Laterality indexes of VOL and NUM showed no significant positive correlations while they both showed significant negative correlations ($p<0.05$) in six connected areas, mainly fronto-temporal.

Conclusions: This study provides first evidence of a significant correlation between brain lateralization of diffusion indexes and clinical severity in toddlers with a clinical diagnosis of ASD. Significant correlations mainly involved

regions within the fronto-temporal circuits, known to be crucial for socio-communicative skills. It is of interest that most correlations were negative, suggesting an inversion of the typical left–right asymmetry in subjects with most severe clinical impairment.

**103.005** Reciprocal 16p11.2 Microduplication and Microdeletion Carriers Show Opposing Structural Brain Changes, and Differential Effects on Cortical Thickness Vs Surface Area. A. Y. Qureshi*[1], S. Mueller[1], A. Z. Snyder[2], W. Chung[3], E. H. Sherr[4], J. Owen[5] and R. Buckner[1], (1)*Harvard*, (2)*Washington University School of Medicine*, (3)*Columbia University*, (4)*University of California, San Francisco*, (5)*UCSF*

Background: Over 100 monogenic disorders and over 40 recurrent copy-number variations (CNVs) have been implicated in ASD. In face of this genetic heterogeneity, the Simons VIP Consortium took a genetics-first approach to studying ASD and neurodevelopmental disorder by recruiting a large number of subjects with a recurrent ~600 kb (BP4-BP5) 16p11.2 microdeletion or microduplication. In ASD this CNV occurs at a frequency of 0.76%. Notably, mirror phenotypes occur with deletion carriers with larger head sizes and obesity, whereas duplication carriers can have smaller head sizes and low body mass index. Differences in head circumference in 16p11.2 carriers are of particular relevance to autism, since macrocephaly is more common in autism. This may suggest that early brain overgrowth is fundamental to the pathobiology of some forms of autism.

Objectives: 16p11.2 may serve as a model to examine the early overgrowth hypothesis in autism. To date, there has been no study evaluating brain structure of 16p11.2 microdeletions and microduplications. It is unknown whether the change in head size is due to a global increase in cortical and/or subcortical volumes or whether there is differential growth in brain structures. Examination of structural morphometry may provide insight into the mechanism for aberrant neurocognitive development in 16p11.2

Methods: Twenty-five pediatric deletion carriers and 43 pediatric controls (ages 8 to 17), as well as 19 adult duplication carriers and 43 adult controls (ages 19 to 63) were recruited from the Simons VIP study. All structural MR imaging was performed at UCSF and CHOP and then analyzed at Harvard using FreeSurfer version 4.5.0 software package.

Results: Cortical and subcortical estimates show opposing effects between duplication and deletion carriers. Deletion carriers have increased volume compared to control subjects, while duplication carriers show decreased volume. This difference was observed in intracranial volume, brain volume, cortical gray matter volume, and cortical white matter volume ($p < 0.001$). Cerebellar volume and thalamic volume were significantly different ($p < 0.05$), and hippocampus/amygdale volumes approached significant difference ($p < 0.06$). Allometric scaling of cortical gray matter versus intracranial volume alleviates concern that age-dependent effects may be confounded with the effect of CNV, thus confirming the reciprocal nature of the brain volumes in deletion vs. duplication carriers. Further analysis showed strikingly differential effects on the components of gray matter volume: surface area was significantly different between cases and controls ($p < 0.005$), whereas no difference was found on estimates of cortical thickness ($p > 0.24$).

Conclusions: The effect from 16p11.2 is dependent on the dosage of the CNV: 1 copy (deletion), 2 copies (controls), or three copies (duplication). This CNV has highly significant effects on brain volume, and 16p11.2 differentially affects cortical surface area but not the thickness of the cortical ribbon. This suggests that 16p11.2 may influence an early stage of embryonic brain development.

**103.006** High Diagnostic Prediction Accuracy for ASD Using Functional Connectivity MRI Data and Random Forest Machine Learning. C. P. Chen*[1], B. A. Bailey[2], C. L. Keown[3] and R. A. Müller[1], (1)*Dept. of Psychology, San Diego State University*, (2)*San Diego State University*, (3)*University of California San Diego*

Background: Although considered a neurological disorder, ASD is diagnosed based on behavioral criteria because unique brain biomarkers are not known. Mounting evidence from functional connectivity MRI (fcMRI) suggests aberrant connectivity in ASD involving multiple brain networks. Machine learning provides promising tools for diagnostic classification (ASD vs. typically developing [TD]) and for the identification of complex biomarkers.

Objectives: To predict diagnostic status based on large-sample resting state fcMRI data, using random forest (RF) feature selection in an attempt to identify functional connectivity biomarkers of ASD.

Methods: We used resting state fMRI data from 252 low-motion participants (126 ASD, 126 TD) from the Autism Brain Imaging Data Exchange (ABIDE), matched on age, nonverbal IQ, and head motion. FMRI data were motion and field map corrected, aligned to high-resolution anatomicals, standardized to the MNI152 template, and blurred to a 6mm global full-width-at-half-maximum. Six rigid-body motion parameters and signal from white matter and ventricles were modeled as nuisance regressors. Time points with motion >.25mm (and their neighbors) were censored. We chose 220 regions of interest (ROIs) from Power et al. (2011), using 10mm spheres to extract an average signal from each. For each ROI pair, a feature was defined as the functional connectivity (signal correlation; 24090 total features). Implementing the randomForest package in R for feature selection, we used the top features for binary classification. Random forest is a multivariate machine learning method that uses an ensemble of classification and regression trees (CART) and aggregates their results, capitalizing on linear and non-linear interactions of brain networks and connectivity. RF minimizes overfitting and contains an internal validation step by selecting bootstrap samples to build the tree and then using the 'out of bag' (OOB) sample to determine error and variable importance (analogous to leave-one-out and other cross-validation procedures).

Results: Using RF feature reduction, we examined the top 100 features with highest importance scores. OOB errors reached a plateau at ≤15% with >40 features. A maximum classification accuracy of 90.1% (OOB error 9.9%) was achieved using 69 features, with 89.8% sensitivity and 90.4% specificity. Selected connections had an average Euclidean distance of 74.1mm, and were primarily inter-network (85.5%) as opposed to intra-network (14.5%). Of the connections with between group difference at $p<.05$, 80% were underconnected (ASD < TD) and 20% were overconnected. Of the ROIs included in these informative connections, 24% were in the default mode, 13% in somatosensory/motor, and 10% in visual networks.

Conclusions: A 90% classification accuracy suggests that resting state functional connectivity may be a promising source of ASD biomarkers. Selected most informative features were overall consistent with the literature, implicating primarily long-distance connectivity, in particular of default mode, but also sensorimotor networks. Informative connections were predominantly (but not exclusively) characterized by underconnectivity in ASD.

**103.007** Correlations of Quantitative EEG with Language and Cognitive Functioning As Biomarkers of Autism Spectrum Disorders. K. McEvoy* and S. S. Jeste, *UCLA*

**Background**: Quantitative electroencephalography (QEEG) allows for analysis of the strength of neural activity at different natural frequencies, and its use as a biomarker for various aspects of autism spectrum disorders (ASD) has shown particular promise.

**Objectives**: In order to determine QEEG's potential as a biomarker of language and cognitive functioning in children with an ASD, we investigated EEG power in the theta (4-8 Hz), alpha (8-12 Hz), and gamma (35-45 Hz) frequency bands of preschool-aged children (ages 26-75 months) with an ASD and typically developing (TD) controls. Our objectives were to: (1) investigate if theta, alpha, and/or gamma power correlate with language and IQ in children with an ASD, and (2) determine if band power can be used as a biomarker of language and/or cognitive functioning for children or subgroups of children with an ASD. This is the first study to use such a heterogeneous population of children with an ASD, and as such is well suited to investigate subgroups within the disorder.

**Methods**: Two minutes of resting-state EEG data were recorded from 69 children with an ASD and 48 typical developing controls. Children were at rest while watching a video of bubbles. EEG recordings were acquired at 250 Hz using a 128-electrode Hydrocel Geodesic Sensor Net System (EGI Inc.). Offline processing of each child's EEG included, band pass filtering, segmenting into one second epochs, and examining for artifact contaminated data. Using Matlab (Matlab Inc.), absolute and relative power were calculated for theta, alpha, and gamma bands in order to obtain a measurement of the power spectral density (PSD) for each frequency band. Depending on the age and developmental level of each child, a

combination of the Mullen Scales of Early Learning (MSEL), Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV), the Differential Abilities Scale (DAS-II), Preschool Language Scale-4 (PLS-4), and Clinical Evaluation of Language Fundamentals (CELF) were administered to all children.

**Results**: Both the TD and ASD groups displayed significant differences in power correlations with language and IQ. Major group differences included: IQ correlated *positively* with frontal theta power for the TD group, but *negatively* for the ASD group; non-verbal IQ correlated *positively* with posterior alpha power, but only for the TD group; and both IQ and language measures correlated with regional gamma power, but correlations were *positive* for the TD group and *negative* with the ASD group. In fact, significant correlations for the TD group were predominantly in the *positive* direction, whereas correlations for the ASD group were in the *negative* direction.

**Conclusions**: Correlations of QEEG band power with language and cognitive functioning have the potential to aid in distinguishing children with an ASD from TD children.

**103.008** Neural Mechanisms and Biomarkers of Response to Pivotal Response Treatment. P. Ventola*[1], H. Friedman[2], D. Oosting[2], L. C. Anderson[3], C. Cordeaux[2], R. Doggett[2], C. E. Mukerji[2], M. Coffman[4], J. Wolf[2], B. C. Vander Wyk[2], J. McPartland[2] and K. A. Pelphrey[2], (1)*Yale Child Study Center*, (2)*Yale University*, (3)*University of Maryland*, (4)*Virginia Polytechnic Institute and State University*

**Background:** Pivotal Response Treatment is an empirically supported behavioral treatment for ASD that improves social communication skills. Research validating PRT has relied on overt behavioral measures as outcome data, which demonstrate improvements in targeted skills but provide minimal insight into underlying mechanisms of change. Functional magnetic resonance imaging (fMRI) provides us with the opportunity to identify the neural mechanisms underlying the behavioral improvements resulting from PRT.

Our research team has used fMRI to characterize the fundamental components of the neural circuitry supporting social perception in the typically and atypically developing human brain. The social stimuli we utilized, comprised of point light displays of biological motion, have been effectively used to identify brain (Kaiser et al., 2010) and behavioral (Klin et al., 2009) signatures of disruptions in social motivation.

**Objectives:** This is the first study to demonstrate the clinical efficacy of a short-duration, PRT program versus a waitlist control condition. The outcome measures include standardized assessments, so we are able to demonstrate improvement in specific behaviors and collateral improvements in adaptive functioning and broad-based social communication skills (e.g., social cognition). Additionally, we are able to identify neural-systems-level mechanisms by which PRT improves social communication using a well-tested biological motion neuroimaging paradigm.

**Methods:** Twelve children, aged 4-6 years, with ASD received 8 hours per week of PRT for 4 months. Six of these children were also first included in a waitlist control condition. Clinical outcome was assessed using the SRS, ADOS, Vineland-II, and clinical observation. Participants completed an fMRI before and after treatment. The children in the waitlist control condition completed an additional fMRI four months prior to treatment. The paradigm was a passive viewing task (328 secs) of point light displays, consisting of 6 biological motion and 6 scrambled motion blocks, presented in an alternating-block design.

**Results:** The participating children exhibited significant behavioral improvement per clinician assessment and parent report (e.g., on the Vineland-II, improvements in receptive communication, daily living, play, and coping skills were significant at $p < .05$; SRS Total raw score decreased (improved) by an average of 22.3 with a standard error of 7.8). In addition, the children showed increased activation to social stimuli in brain regions underpinning social function, specifically the left ventrolateral prefrontal cortex (vlPFC), left dorsolateral prefrontal cortex (dlPFC), ventromedial prefrontal cortex (vmPFC), right posterior superior temporal sulcus (STS), and right fusiform gyrus (FFG) (beta difference > .5, $k = 40$).

**Conclusions:** The current research introduces an innovative approach for studying response to an empirically supported behavioral treatment by integrating behavioral and neural systems level results. PRT results in significant gains in social

communication and adaptive skills even within the context of a short-duration program, which can dramatically increase access to care. Furthermore, neural systems supporting social perception are malleable in children with ASD. The children demonstrated increased activation in key brain regions involved in social processing after conclusion of the treatment program. Further understanding of neural systems level mechanisms will inform predictions of response to treatment and refine interventions toward the goal of personalized care.

## 104 Gesture, Speech and Social Communication

*Organizer:* C. Lord *Weill Cornell Medical College*

**104.001** Deictic but Not Conventional Gestures Predict Children's Vocabulary One Year Later. S. Ozcaliskan*[1], L. B. Adamson[2] and N. Dimitrova[2], (1)*Georgia State University*, (2)*Georgia State Unviersity*

**Background:** Children refer to objects with their hands (e.g., point at cat) before they can produce verbal labels for these objects ("cat"; Bates et al., 1979). Importantly, the onset of such deictic gestures predicts the onset of similar spoken words in typically developing (TD) children, showing a strong positive relation between early deictic gestures and early words (Iverson & Goldin-Meadow, 2005). Children with autism spectrum disorder (ASD) show difficulties in early gesture use, particularly in pointing (Mundy et al., 1986); they also often show prolonged delays in producing words and use fewer words compared to TD children.

**Objectives:** In this study, we ask how the delays and difficulties that we observe in the vocabulary development of children with ASD are related to gesture production. We hypothesized that early production of deictic gestures would be more affected than the production of other gesture types (e.g., conventional, iconic) and that variations in deictic gesture production but not other gesture types would be related to later language.

**Methods:** We tested this question by observing 23 18-month-old TD children and 23 30-month-old children with ASD—comparable to TD children in productive vocabulary, as they interacted for 20 minutes with their mothers in a semi-naturalistic observational protocol (Communication Play Protocol, CPP). We coded the types of gestures children produced; these included *deictic gestures* (e.g., pointing at an object to indicate an object), *conventional* gestures (e.g., nodding the head to mean 'yes', extending an open palm next to an object to indicate 'give object') and *iconic gestures*(e.g., moving hand forcefully to indicate 'throwing'). Iconic gestures were extremely rare in our data; therefore we only focused on deictic and conventional gestures in our analysis. In addition, we assessed children's spoken vocabulary—both tokens and types of words produced, during a second CPP performed one year later.

**Results:** We found that children with ASD showed significant deficits in their production of **deictic**, but ***not*** **conventional** gestures: compared to TD children, fewer children with ASD produced deictic gestures (56% vs. 100%, $X^2(1) = 12.78$, $p<.001$), also producing them at significantly lower rates (Kruskall–Wallis, $H(1)=12.49$, $p<.001$). Importantly, the production of deictic gestures predicted the size of children's vocabulary both for word tokens ($r = .69$, $p<.01$) and word types ($r=.68$, $p<.01$) one year later; but no such predictive association was found for conventional gestures and vocabulary size.

**Conclusions:** These results show that deictic gesture is a fundamental aspect of the language learning process in children with ASD—as it is in TD children, predicting children's spoken language development. Our results further suggest that it is *not* gesturing per se, but the production of a particular gesture type, namely deictic gesture, that serves as a stepping-stone for subsequent vocabulary development. Children's deictic gestures may play this important role by helping children establish a joint focus that the caregiver can then elaborate with language.

**104.002** Gesture Production As a Predictor of Outcomes for Children with Autism in Early Intervention. B. Harrison*, L. Bennetto, T. Smith, M. Sturge-Apple and R. Klorman, *University of Rochester*

Background:
Predictors of treatment outcomes for children with autism spectrum disorder (ASD) have been extensively studied, but less is known about individual differences that may explain variation in response to early intervention. Given that specific gestures, such as pointing for joint attention, presage subsequent language acquisition in children with and without ASD, the present study characterized differences in gesture and tested whether these aid in predicting outcomes in ASD.

Objectives:
This study used a multi-method approach for measuring gesture production as a predictor of treatment outcomes for children with ASD enrolled in early intensive behavioral intervention. This study also derived latent constructs to represent gesture production and treatment outcomes.

Methods:
Participants included 71 children with ASD who received early, intensive behavioral intervention for a period of two years (mean age at intake=3.28 years; 60 males) as part of a study that evaluated predictors of intervention response. Gesture production was represented with scales from the MacArthur Communicative Development Inventory (Fenson et al., 1993), the Early Social Communication Scale (Mundy & Hogan, 1986), and items from the Autism Diagnostic Interview–Revised (Lord et al., 1994). A coding system was also developed to capture the diversity of gestures children produced with their gestures during the Autism Diagnostic Observation Schedule. Treatment outcomes were represented with the Mullen Scales of Early Learning (Mullen, 1995), Vineland Adaptive Behavior Scales (Sparrow et al., 1984), and the Autism Diagnostic Observation Schedule (Lord et al., 2000). Structural equation models tested how gesture at intake predicted variability in outcome change at both follow-up assessments.

Results:
A latent construct representing gesture was successfully obtained $\chi2(1)=.21$, $p=.65$, CFI=.99, RMSEA=.01, and used to evaluate gesture's relationship with treatment outcomes. Treatment outcomes were best represented as a latent construct with scores from the Mullen and Vineland scales. A change regression model (McArdle, 2009) indicated that gesture and outcome significantly co-varied at the intake assessment such that higher scores on the outcome construct were associated with higher levels of gesture, $r=.73$, $p<.001$. Moreover, gesture significantly predicted variability in change such that participants with higher intake levels of gesture showed greater amounts of improvement on the outcome construct at both the Year 1 ($\beta=.50$, $p=.002$) and Year 2 ($\beta=.42$, $p=.01$) assessments. Gesture production remained a significant positive predictor of the variability in change at each assessment (Year 1: $\beta=.41$, $p=.009$; Year 2: $\beta=.36$, $p=.03$) when caregiver report of speech production was included as a concurrent predictor.

Conclusions:
This study showed that initial differences in gesture production could be used to predict variability in treatment outcome. Participants who began treatment with higher gesture production showed greater gains in outcome, and this effect remained even after controlling for concurrent speech. Given that early intervention strives to improve the functioning of children with ASD during a period marked by greater plasticity and a heightened possibility for accelerating the rate of change (Warren et al., 2011), these results suggest that higher levels of gesture may magnify the benefits of early intervention for children with ASD.

**104.003** When Pronouns Are Points: Investigating Reference to Self and Other in Signing ASD Children. A. Shield*, *Boston University*

Background:

Children with autism spectrum disorder (ASD) have difficulty with personal pronouns, especially first- and second-person forms, either reversing them (e.g., Kanner, 1943; Bartak & Rutter, 1974) or avoiding their use altogether, instead referring to themselves or others by name (Lee, et al., 1994). The personal pronouns 'I/me' and 'you' in American Sign Language (ASL) are points with the index finger to self and other, respectively. Thus, unlike spoken language pronouns, they transparently pick out the person to whom they refer. Could this characteristic of sign pronouns aid their acquisition by deaf signing children with ASD? Or, will deaf signing children with ASD *reverse* or *avoid* pronouns like hearing ASD children do?

Objectives:

This study aimed to test the pronoun production skills of deaf ASD children in comparison to a group of typically-developing (TD) deaf children.

Methods:

Children's receptive language ability and nonverbal IQ were measured using the ASL Receptive Skills Test (Enns, et al, 2013) and the Test of Nonverbal Intelligence, Fourth Edition

(TONI-4). ASD diagnosis was verified using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2; Lord, et al., 2012).

Naturalistic language sample: The ADOS evaluation was coded for self-other reference and pointing behavior.

Elicitation: The experimenter took a picture of the child using an iPad, showed him/her the picture, and asked in ASL *"who is this?"* The experimenter then showed the child a picture of the experimenter and asked again in ASL *"who is this?"*

Results:

Sixteen deaf children with ASD (5 females, all of deaf parents) and 18 typically-developing (TD) deaf children (11 females, all of deaf parents) participated. The two groups were matched for chronological (ASD: ages 5;1-14;4; $M_{age}$=9;9, SD=2;6; TD: ages 6;6-12;9; $M_{age}$=9;2, SD=1;10) and mental age (ASD: $M_{age}$=9;3, SD=3;4; TD: $M_{age}$=9;9, SD=3;4); there were no significant group differences ($p$=.42 and .63, *ns*, for chronological and mental age, respectively). On the first-person pronoun task, 16 TD children, but only 5 ASD children, produced the ASL 1st-person pronoun; two TD children and 11 ASD children responded by signing their name. Fisher's Exact Test revealed a significant difference between the TD and ASD groups, $p$<.01. On the second-person pronoun task, all 18 TD children, but only 8 ASD children, produced the ASL 2nd-person pronoun. The ASD children fingerspelled the experimenter's name or responded idiosyncratically, signing "boy", "man", or "doctor". The group difference was again significant, $p$<.01. An analysis of the naturalistic language sample showed that all ASD children produced index-finger points, suggesting that the ability to point was not specifically impaired. However, production of pronouns was strongly correlated with language level, $r$(32)=.51, $p$<.01, but not mental age ($r$(32)=.11, *ns*) or chronological age ($r$(32)=.004, *ns*). No pronoun reversals were found in either the elicitation tasks or naturalistic language samples.

Conclusions:

Deaf ASD children were found to exhibit pronoun *avoidance*, just as hearing ASD children do, but not pronoun *reversal*. Pronoun production was strongly correlated with language level, but not with mental or chronological age. Personal pronouns appear to pose a particular challenge to ASD learners in both sign and speech.

**104.004** Communication Growth in Minimally Verbal Children with Autism. C. Mucchetti*[1], A. P. Kaiser[2] and C. Kasari[1], (1)*University of California Los Angeles*, (2)*Vanderbilt University*

**Background:** Approximately 30% of children with autism spectrum disorders (ASD) are minimally verbal past age 5. School-aged minimally verbal children with ASD are often excluded from research so information on their communication development is limited. Interventions for this population focus on discrete speech skills, often requesting in response to prompts, with limited attention to how children engage in reciprocal communication and how they initiate communication. This study examines how minimally verbal children with ASD initiate communication interchanges (CI) over the course of six-month intervention, and what communicative functions those CI serve. CI are rounds of talk between partners serving a single communicative function (Ninio et al., 1994). The developmental course of CI has been documented in typically developing children and children with language impairment (Ninio et al., 1994, Snow et al, 1996).

**Objectives:** This study seeks to investigate child initiations of CI over time, as well as document communicative functions observed.

**Methods:** Participants included 53 minimally verbal children with ASD from an intervention study, using a blend of two existing interventions - Joint Attention, Symbolic Play, Engagement and Regulation (JASPER) (Kasari et al, 2006) and Enhanced Milieu Teaching (EMT) (Kaiser, 1993). Participants were randomized to Speech (spoken language only) or AAC (spoken language plus augmentative/alternative communication device) versions of the intervention. Forty-eight sessions occurred, twice per week (one hour each) over the six months.

Intervention sessions were videotaped and participant communication was transcribed at entry and monthly over the course of intervention (seven time points). These transcripts were coded

for CI and analyzed for proportion of child initiations per session and communicative functions.

**Results:** Children in both treatment groups showed significant growth in the proportion of child initiated CI over the course of intervention ($f$=13.81, $p$=.0002). Average proportion of child initiation CI at entry was 53% ($SD$ = 25%) which increased to 71% ($SD$ = 14%) by the end of intervention. There was no effect of treatment group ($f$=.27, $p$=.60) or site ($f$=2.19, $p$=.11) on the growth trajectory. CI served a variety of communicative functions, and these proportions did not change significantly over the course of intervention. CI for the function of negotiating (possession of objects or activities) was the largest proportion, averaging 48% over time. Discuss functions (joint attention, fantasy play, thoughts) accounted for an average of 31% of CI. Establishing mutual attention was used rarely, accounting for an average of 5% of CI and the remaining CI had an unknown or ambiguous function (16%).

**Conclusions:** This study highlights the ability of children with ASD who are minimally verbal to initiate communicative interactions serving a variety of functions when provided the opportunity to do so. Beyond requesting, children participated in communication for the purpose of discussing and sharing attention. In addition, the findings demonstrate growth in children's frequency of initiations through brief targeted intervention.

**104.005** Development of a Novel Functional Social Communication Classification Tool for Preschool Children with ASD: Preliminary Assessment of Intra- and Inter-Rater Agreement.

B. M. Di Rezze*[1], M. Cousins[2], L. Zwaigenbaum[3], M. J. C. Hidecker[4], C. Camden[1], M. Law[1], P. Stratford[1] and P. Rosenbaum[5], (1)*McMaster University*, (2)*CanChild Centre for Childhood Disability Research*, (3)*University of Alberta*, (4)*University of Wyoming*, (5)*CanChild Centre, McMaster University*

Background: The Autism Classification System of Functioning: Social Communication (ACSF:SC), a content-valid tool for preschoolers, describes functional ability in social communication, the hallmark challenge in ASD. Understanding the range of social communication abilities is necessary to create a common language, to characterize and to describe groups of children with similar abilities. The five levels of ACSF:SC describe social communication of preschool children with ASD (level 1=most functional to level 5=least functional). Familiar raters select the level that best matches the child's usual (i.e., typical) as well as best (i.e., capacity) social communication.

Objectives: To examine intra- and inter-rater agreement of parents and professionals using the ACSF:SC.

Methods: We recruited parents of preschool children with ASD (age 3.0 to <5.11 years), who nominated two professionals working with their child (who were then assigned to one of two rater groups [cohorts]). Participants completed the ACSF:SC on two occasions. Demographic data were collected about the child, the rater's relationship to the child, and frequency of observations of the child's social communication. Quantitative and qualitative data were collected through a thought process questionnaire (TPQ) that evaluated the rating process, utility and perceptions of using the ACSF:SC. Percent agreement scores described the results from the TPQ, intra-rater (from Time 1 to Time 2) and inter-rater agreement.

Results: Eleven sites in Canada recruited parents. Characteristics of child sample (n=29): mean age = 4.18; 90% males. Nominated professionals included clinicians (n=19) and pre-school educators (n=18).

On several items from the TPQ, 88%-100% of raters reported following User Guide instructions with the ACSF:SC. When asked about the comprehensibility (e.g., ease of understanding level descriptions) and utility (e.g., ease of matching child descriptions to abilities) of the ACSF:SC guide, 77%-92% of parents and 92-97% of professionals responded positively. All five ACSF:SC levels were represented although there were fewer children in levels 1 and 5.

Intra-rater agreement for capacity (C) and typical (T) performance from Time 1 to Time 2 were: parents (n=17) 65%(C) and 71%(T); professionals (cohort #1, n=20) 67%(C) and 50%(T); and professionals (cohort #2, n=7) 86%(C) and 71%(T).

Inter-rater agreement for capacity (C) and typical (T) performance at Time 1 showed: parent and professionals (cohort #1) 26%(C) and 37%(T); parent and professionals (cohort #2) 45% (for both C and T); and professionals (cohort #1 and cohort #2) 38.5%(C) and 46%(T).

Conclusions: The raters' high level of comprehension on the use and utility of the novel ACSF:SC is encouraging for the future acceptability and adoption of the tool. The context of where and with whom social communications occur is an important consideration for identifying a child's level of functional ability. This may explain differences in time 1 inter-rater agreement between professionals, as well as between parents and professionals. Intra-rater agreement ratings were good for parents and professionals. Once inter-rater agreement and validity are established, ACSF:SC can be used in research and clinical practice to examine abilities over time, whether interventions change these abilities, and to identify contextual factors that may influence different social communication abilities.

**104.006** A Novel Teacher Implemented Protocol to Assess Early Social Communication Skills and Play in Preschool Children with Autism. S. Y. Patterson* and C. Kasari, *University of California Los Angeles*

Background:

Initiations of early nonverbal social communication skills including gestures to request (behaviour regulation) and share (joint attention) as well as play skills are fundamental to young children's development. Yet, educators and community practitioners have limited access to validated tools to assess these foundational skills and select developmentally appropriate skill targets.

Objectives:

The assess the feasibility and validity of a novel teacher implemented brief assessment designed to capture the presence of preschool children's nonverbal social communication and play skills in classroom settings and facilitate teachers' selection of developmentally appropriate target skills for students.

Methods:

Participants. Six teachers and two paraprofessionals from six public preschool classrooms administered the assessment with a total of 68 preschool students with autism who were enrolled in a larger intervention study.

Measures. Three assessments were administered at entry into the larger study including two well-established protocols used in research: the Early Social Communication Scale (ESCS: Mundy et al., 2003) and Structured Play Assessment (SPA: Ungerer & Sigman, 1981). In addition, a novel assessment was designed to function as a brief protocol of the ESCS and SPA for use by teachers to identify skill targets in core areas of early development.

Outcomes. Children's spontaneous initiations of joint attention (including coordinated joint looks, points, shows, and gives), behaviour regulation (give and point to request) as well as four levels of play skills (simple, combination, pre-symbolic, and symbolic) were examined. Teachers recorded the presence or absence of the behaviours on a three-point scale (never, once, two or more).

Results:

On average, teachers delivered the novel assessment with 86.57% fidelity (*SD*= 8.15%). Logistic regression was applied to examine the probability of teachers' agreement of their in vivo selection of children's skill targets with the researcher's target selected after review of the videotaped administration of the brief assessment. The probability of skill target agreement between each of the eight teachers and the researcher varied by skill domain including: JA skills (0.40-1.00), BR skills (0.30-1.00), and play skills (0.40-0.60). Agreement on JA skills and BR skills was greater than chance (JA: $chi^2$ (1)= 4.76, $p<0.05$; BR: $chi^2$ (1)= 11.53, $p<0.01$) while play was not.

Further, agreement between researcher selected JA target skills from the brief assessment and JA targets selected from the ESCS was above chance ($chi^2$ (1)= 5.06, $p<0.05$) while agreement on BR targets was not ($p=0.32$). Finally, agreement between the researcher selected play target and the target obtained from the SPA was significantly above chance ($chi^2$ (1)= 5.06, $p<0.01$).

Conclusions:

Although lower agreement occurred on BR target selection, findings from this preliminary study indicate that similar JA and play targets were obtained from the brief assessment and the established research protocols. Several factors related to variability in BR will be discussed including ESCS administration fidelity and prompting protocols.

Further, findings indicate teachers could learn to administer the assessment and often select accurate JA and BR target skills yet agreement not above chance was found for play. Further training regarding developmental play levels may enhance teachers' accurate identification of play targets.

**104.007** Respiratory Sinus Arrhythmia As a Predictor of Language Outcomes in Initially Nonverbal Children with Autism. L. R. Watson*[1], P. J. Yoder[2], J. E. Roberts[3] and G. T. Baranek[1], (1)*University of North Carolina at Chapel Hill*, (2)*Vanderbilt University*, (3)*Barnwell College*

Background:

Absence of functional spoken language beyond the preschool years places children with autism spectrum disorders (ASD) at grave risk for poor social and adaptive outcomes in adulthood. Although considerable research has provided insight into predictors of later spoken language outcomes among children with ASD, minimal attention has been given to biologically-based predictors. Examining such predictors may provide insight into underlying mechanisms accounting for variable spoken language outcomes in ASD. Porges (1994, 2007) proposed that respiratory sinus arrhythmia (RSA) indexes influences of the neocortex on a complex social engagement system that includes the vagus. We have been especially interested in attention to child-directed speech (CDS) among children with ASD as a predictor of later language outcomes. Arguably, RSA indexes a key physiological substrate for sustained attention in social contexts. We previously demonstrated that RSA during exposure to CDS accounted for significant variance in expressive language outcomes of preschoolers with ASD that was unexplained by amount of looking at these stimuli (Watson et al, 2010).

Objectives:

To determine the value of RSA during CDS, combined with non-biological variables, in predicting expressive language outcomes in initially nonverbal preschoolers with ASD.

Methods:

Fifty-two initially nonverbal preschoolers with ASD were assessed 5 times in 4-month intervals over 16 months. Expressive vocabulary size was estimated using a parent report tool (i.e., McArthur-Bates Communicative Development Inventory, Words and Gestures), collected at each assessment. Mixed level modeling was used to quantify individual vocabulary growth curves. The Time 5-centered intercept of expressive vocabulary was selected as the outcome measure. Putative predictors, measured at Times 1 and/or 2, included child communicative acts, response to joint attention, consonant inventory, oral-motor skills, motor imitation, vocabulary comprehension, and parent linguistic responsivity, as well as percent of time spent looking at CDS vignettes (3 minutes) and RSA during these vignettes. Based on prior analyses (excluding CDS variables) of unique predictors of expressive vocabulary (Yoder & Watson, in preparation), the final regression model for the current analysis included four putative predictors: child communicative acts, parent linguistic responsivity, percent of time looking at CDS, and RSA during CDS.

Results:

The full model accounted for 36.6% of the variance in expressive vocabulary outcomes, $F(4,46) = 6.6$, $p < .001$. Child communicative acts, parent responsivity, and RSA during CDS each accounted for significant unique variance ($p$s $<.05$), whereas the percent of time spent looking at CDS did not ($p = .42$).

Conclusions:

This study expands on our previous findings to demonstrate that RSA accounts for variance in expressive language outcomes beyond that accounted for by other significant predictors. The physiological substrates underlying attention to CDS appear to influence ongoing development of expressive language. Based on Porges (1994, 2007), children with ASD who have higher RSA during CDS possibly are those experiencing stronger social affiliation. Merely "paying attention" (i.e., looking and presumably listening) to language input may be insufficient for optimal

expressive language development in children with ASD; perhaps instead, the extent to which children process language input as a positive social phenomenon is key to their outcomes.

**104.008** Voice Patterns in Children with Autism Spectrum Disorder: Predicting Diagnostic Status and Symptoms Severity. R. Fusaroli*[1], C. Cantio[2], N. Bilenberg[3] and E. Weed[1], (1)*Aarhus University*, (2)*Odense University Hospital*, (3)*University of Southern Denmark*

**Background:** Individuals with autism spectrum disorder (ASD) tend to have atypical modulation of speech, often described as awkward, monotone, or sing-songy (Shriberg et al., 2001). The patterns may be one of the most robust signals of social communication deficits in ASD (Paul et al., 2005). However, it has proven difficult to determine a consistent set of acoustic features that can account for these perceived differences. Using Recurrence Quantification analysis of acoustic features, Fusaroli et al. (Fusaroli, Bang, & Weed, 2013) demonstrated a high efficacy of identifying voice patterns characteristic of adult Danish speakers with Asperger's syndrome.

**Objectives:** We systematically quantify and explore speech patterns in Danish children (8-12 years) with and without autism. We employ traditional and non-linear techniques measuring the structure (regularity and complexity) of speech behavior (i.e. fundamental frequency, use of pauses, speech rate). Our aims are (1) to achieve a more fine-grained understanding of the speech patterns in children with ASD, and (2) to employ the results in a supervised machine-learning process to determine whether acoustic features can be used to predict diagnostic status and severity of the symptoms.

**Methods:** Our analysis was based on previously-acquired repeated narratives (TOMAL-2 (Reynolds & Voress, 2007)). We tested 25 Danish children diagnosed with ASD and matched controls. Participants had been diagnosed using ADOS and ADI-R and their symptoms assess with SRS and SCQ. Transcripts were time-coded, and pitch (F0), speech-pause sequences and speech rate were automatically extracted. Per each prosodic feature we calculated traditional statistical measures. We then extracted non-linear measure of recurrence: treating voice as a dynamical system, we reconstructed its phase space and measured the number, duration and structure of repeated trajectories in that space(Marwan, Carmen Romano, Thiel, & Kurths, 2007). The results were employed to train (1) a linear discriminant function algorithm to classify the descriptions as belonging either to the ASD or the control group, and (2) a multiple linear regression to predict scores in Social Responsiveness Scale (SRS) and Social Communication Questionnaire (SCQ). Both models were developed and tested using 1000 iterations of 10-fold cross-validation (to test the generalizability of the accuracy) and variational Bayesian mixed-effects inferences (to compensate for biases in sample sizes).

**Results:** While traditional measured did not allow for accurate classification, recurrence measures allowed to define voices as autistic or not with balanced accuracy > 77% ($p<.00001$, CI =71.79%- 81.01%), sensitivity: 79.19%, specificity: 82.37%. Recurrence also allowed to explain variance in the severity of the symptoms: 42.76% ($p<.00001$) for SCQ and 55.80% for SRS ($p<.00001$, 48.18% for Social Consciousness, 53.92% for Social Cognition, 54.46% for Social Communication, 47.18% for Social Motivation and 61,04% for Autistic Mannerism). Autistic voice can be characterized as more regular (i.e. with regularly repeated patterns) pitch and pause use than neurotypical voices,

**Conclusions:** Non-linear time series analyses techniques suggest that there are quantifiable acoustic features in speech production of children with ASD that both distinguish them from typically developing speakers and reflect the severity of the symptoms.

## 105 Interventions: Factors Affecting Feasibility and Outcomes

*Organizer:* D. S. Mandell *University of Pennsylvania School of Medicine*

**105.001** Intervention History of Children and Adolescents with High-Functioning Autism and Optimal Outcomes. A. Orinstein*, M. Helt, E. Troyb, K. E. Tyson, M. L. Barton, I. M. Eigsti, L. Naigles and D. A. Fein, *University of Connecticut*

Background: A study is currently following children and adolescents who have a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for the disorder. These individuals have achieved social and language skills within the average range for their ages and receive little or no school support. Several recent studies suggest that this small subset of children, once diagnosed with ASD,

achieve an "optimal outcome (OO)" (Fein et al., 2013; Sutera et al., 2007; Kelley et al., 2010; & Helt et al., 2008).

Objectives: The present study aimed to retrospectively examine group differences in the intervention history of children and adolescents with OO and those with high-functioning autism (HFA) to determine if specific early interventions are related to optimal outcomes in childhood and adolescence.

Methods: The current study examined intervention histories in 34 individuals with OO and 44 individuals with HFA (ages 8-21 at time of participation), who did not differ on age, sex, nonverbal IQ or family income. Intervention history was collected through detailed parent questionnaires.

Results: Children in the OO group had earlier parental concern ($M$(HFA)=22.0 months, $M$(OO)=16.7 months, $t$=2.00, $p$=.052) and received earlier referrals to specialists ($M$(HFA)=43.9 months, $M$(OO)=26.1 months, $t$=3.79, $p$=.001). The percent of OO children receiving early intervention services was significantly higher than in the HFA group (83 vs. 48%; $\chi^2$(1, n=56)=6.73, $p$=.009), as was the percent who attended preschool (92 vs. 56%; $\chi^2$(1, n=58)=8.70, $p$=.003). Between the ages of 2 and 3 years, OO children received more hours of intervention than the HFA children (ages 2-2.5: $M$(HFA)=4.1, $M$(OO)=14.8, $p$=.006; ages 2.5-3: $M$(HFA)=7.3, $M$(OO)=21.1, $p$=.006). More OO than HFA children received some type of intervention between 2.5 and 3 years of age (HFA=61%, OO=88%, $p$=.025) and during the second year of preschool (HFA=68%, OO=92%, $p$=.031). Specifically, more children in the OO group received Applied Behavior Analysis (ABA) than the HFA group for the following age periods: 2-2.5 years (HFA=4%, OO=40%, $p$=.001), 2.5-3 years (HFA=7%, OO=56%, $p$<.001), 3-4 years (HFA=32%, OO=60%, $p$=.042), and 4-5 years (HFA=25%, OO=72%, $p$=.001). Of the children who received ABA, the intensity did not differ between groups. Children in the HFA group were more likely to have received medication (64% vs. 24%; $p$=.002), especially anti-psychotics (28% vs. 0%; $p$=.007) and anti-depressants (41% vs. 4%; $p$<.001). There were no group differences in the percent of children receiving special diets (HFA=35% vs. OO=23%; $p$=.32) or supplements (HFA=36% vs. OO=40%; $p$=.76).

Conclusions: These data suggest that OO individuals generally receive earlier, more intense interventions and more ABA, while HFA individuals receive more pharmacologic treatments. While the use of retrospective data is a clear limitation to the current study, the substantial differences in reported provision of early intervention, and ABA in particular, are highly suggestive and should be replicated in prospective studies.

**105.002** Eight-Month Parent Outcomes of an Acceptance and Empowerment Training Model in India. T. C. Daley*[1], N. Singhal[2], R. S. Brezis[3], T. Weisner[3] and M. Barua[2], (1)*Westat*, (2)*Action For Autism*, (3)*UCLA*

Background:

Parent training programs rarely have an explicit focus on improving parenting practices, parent problem-solving, or stress management (Brookman-Frazee et al, 2006). Along with increased self-efficacy, these are all aspects of *parent empowerment*. A focus on parent empowerment and psychological acceptance are particularly appropriate for many low and middle income countries, where mothers often shoulder full responsibility for both care and education of their children with disabilities in addition to the demands of the family and household. In addition, there is often a deeply entrenched belief that parents should not question teachers and other professionals. Teaching parent skills and increasing parent knowledge alone is not sufficient to shift these powerful dynamics. The Parent Child Training Program (PCTP) was developed in India in 2000 with parental acceptance of the child and empowerment as explicit program goals. The program additionally aims to provide practical and theoretical knowledge on autism and behavior management. Training takes place over a 3-month period, with the parent and child attending together. To date, the PCTP has trained over 400 participants.

Objectives:

This study presents eight-month outcomes from a mixed-method evaluation of the PCTP training program. It provides the first data that we are aware of to examine longer-term outcomes of parent training in a developing country.

Methods:

Three consecutive cohorts of families ($n$=48 total) participated in the evaluation. Participants joined from a wait-list and entered on a first-come, first-served basis. Diagnosis was confirmed using the ADOS and SCQ. Both parents were interviewed at the start and end of the 3-month program. Mothers were again interviewed eight months after their completion of the program. Measures consisted of a combination of 1) standardized, Western instruments 2) tools developed specifically for this evaluation, and 3) qualitative data collection.

Results:

Cohorts did not differ in demographic characteristics or baseline outcome measures. The statistically significant gains achieved by the post-test were maintained across all parent outcome measures at eight months, including empowerment, acceptance, knowledge of autism, sense of competence, and decreased stress (all $p$<.001). In addition, parent empowerment significantly increased between the post-test and follow up period (p<.01). Mothers were able to articulate gains they perceived in their children and in their own lives in response to open-ended questions at eight months. These data were coded using standard procedures, and maternal perceptions of change were consistent with the quantitative measures.

Conclusions:

The PCTP was developed specifically to meet the needs of families in India, where disability remains highly stigmatizing and services are limited. Using both standardized measures and those developed for this study, the current evaluation provides an estimate of project impacts in key parent outcomes eight months following the completion of a training program. The acceptance and empowerment focus of this model offers a novel way to conceptualize parent training, adds value to knowledge and behavioral training alone, and has high relevance for families in situations where cultural, economic and other contextual factors may be similar to those in India.

**105.003** Emotion-Based Social Skills Training: A Controlled Intervention Study in 55 Mainstream Schools for Children with Autism Spectrum Disorder.

B. J. Ratcliffe*[1], M. Wong[1], D. Dossetor[2] and S. C. Hayes[3], (1)*Children's Hospital at Westmead*, (2)*Sydney Children's Hospital Network*, (3)*University of Sydney*

Background:

Children with Autism Spectrum Disorder (ASD) have significant difficulties with emotional understanding and emotion regulation. However, there is a dearth of evidence-based social-emotional programmes for children with ASD in schools. Emotion-based Social Skills Training (EBSST; Wong, Lopes & Heriot, 2010; Ratcliffe, Grahame & Wong, 2010) is a theory-based, developmentally appropriate group intervention which aims to enhance social-emotional skills in children across the Autism Spectrum.

Objectives: This study aimed to evaluate the effectiveness of delivering EBSST to children with ASD, their parents and teachers by school counsellors in schools using a quasi-experimental treatment versus control group design. It was hypothesized that children in the treatment group would improve on teacher and parent report measures of emotion skills, social skills and mental health, across time (pre-treatment, post-treatment, and 6 month follow-up) compared to the control group.

Methods: Fifty five school counsellors from government schools in NSW, Australia nominated themselves and children in their schools to participate. School counsellors were trained in one of two manualised versions of EBSST: EBSST for High Functioning Autism and Asperger's Syndrome (HFA/AS) or EBSST for ASD and Mild Intellectual Disability (ID). 331 participants with a confirmed or suspected ASD aged 6–13 years were enrolled in the study. Of those, 161 participants were in the treatment group (106 HFA/AS; 55 ASD and Mild ID) and 170 participants were in the control group(111 HFA/AS; 59 ASD and Mild ID).

Parent and teacher questionnaires for emotional competence (Emotions Development Questionnaire, Wong, Heriot & Lopes, 2009), social skills (Social Skills Improvement System, Gresham & Elliott, 2008) and mental health (Strengths and Difficulties Questionnaire, Goodman, 1997; Developmental Behaviour Checklist, Einfeld & Tonge, 2002) were completed to measure change across time. Children in the

treatment group received 16 sessions of EBSST, delivered by their school counsellor in small groups of 3-8 children. Sessions were divided into three modules over three school terms with a booster session at six month follow-up. Teachers and parents also received two EBSST sessions per module and a six month booster session in separate groups

Results: EBSST significantly improved teacher reported emotional competence for both children with ASD with HFA/AS and Mild ID and the effect size was large. This improvement was sustained at 6 month follow-up. Significant improvements in teacher reported social skills were also found for children with HFA/AS when controlling for pre-treatment child mental health. There were no significant differences between treatment and control groups on parent reported emotional competence, social skills or mental health.

Conclusions:

This study is the first large-scale investigation of a theoretically-based social-emotional treatment programme for children with ASD, delivered by school counsellors in mainstream Australian schools. Results suggest EBSST improves emotional competence and social skills at school for children with HFA/AS and ASD and mild ID and that treatment gains are maintained over time. There are several possible explanations for the lack of parent reported treatment gains. This study provides a valuable basis for future research and development.

**105.004** Cognitive Enhancement Therapy for Adults with Autism Spectrum Disorder: Results of an 18-Month Feasibility Study. S. M. Eack*[1], D. P. Greenwald[2], S. S. Hogarty[2], M. Y. Litschge[2], C. A. Mazefsky[2] and N. J. Minshew[2], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

**Background:** Adults with autism spectrum disorders (ASD) experience significant disability due to pervasive social and non-social cognitive impairments. Despite the growing evidence of the neurobiologic basis of these deficits, comprehensive interventions designed to remediate the core cognitive impairments experienced by adults with ASD have yet to be developed or tested.

**Objectives:** The purpose of this research was to adapt and preliminarily test an integrated social and non-social cognitive rehabilitation intervention that has shown significant benefits in patients with schizophrenia, Cognitive Enhancement Therapy (CET), to adults with autism spectrum disorders.

**Methods:** A total of 14 verbal adults with ASD were recruited for an 18-month uncontrolled pilot study of CET. Treatment adherence data were collected continuously along with measures of treatment satisfaction to assess the feasibility and acceptability of CET in this population. In addition, comprehensive measures of neurocognitive and social-cognitive functioning were collected prior to treatment, and at 9 and 18 months of treatment to provide preliminary estimates of potential efficacy.

**Results:** In total, 11 of 14 (79%) participants completed the entire 18-month trial. Participants uniformly endorsed high rates of satisfaction with CET. Pre-treatment data collection indicated significant and broad levels of cognitive impairment among participants, despite intact intelligence scores. After 18 months of treatment, large and significant levels of cognitive improvement were observed. Overall neurocognitive improvement was large ($d$ = 1.40), with effect sizes for individual domains ranging from $d$ = .43, $p$ = .034 (verbal learning and memory) to $d$ = 1.22, $p$ < .001 (processing speed). Social-cognitive improvement was also considerable ($d$ = 2.00, $p$ < .001). In addition, preliminary evidence suggested that these improvements translated into large and significant gains in social adjustment ($d$ = 2.29, $p$ < .001), including vocational and interpersonal domains.

**Conclusions:** CET is a feasible and acceptable approach to cognitive rehabilitation in verbal adults with ASD that shows promise for remediating the core cognitive deficits that limit adaptive function and behavior in this population. The results of an ongoing randomized-controlled trial to evaluate efficacy are eagerly anticipated.

**105.005** Intervention Affects the Families of Adolescents with Autism Spectrum Disorders: Group and Individual-Level Analyses of Parent Stress, Efficacy, and Family Disruption. J. S. Karst, S. Stevens, K. A. Schohl, B. Dolan and A. V. Van Hecke*, *Marquette University*

*Background:* The difficulties of children with Autism Spectrum Disorders (ASD) affect caregivers across a variety of domains, increasing stress and decreasing feelings of parenting

efficacy. The impact of having a child with ASD appears to reverberate throughout the entire family system. Interventions for ASD do not necessarily ameliorate, and may even exacerbate, these family concerns. Thus, comprehensive evaluation of interventions should include assessment of family domains. The Program for the Education and Enrichment of Relationship Skills (PEERS; Laugeson & Frankel, 2009) is a manualized, evidence-based, social skills training intervention for adolescents with ASD. Parents participate in a concurrent, separate group designed to teach PEERS concepts to parents and generalize teen practice of skills outside of group. Though several studies have suggested positive outcomes for adolescents following PEERS, studies have not yet evaluated parent and family outcomes.

*Objectives:* The purpose of this study was to understand how participation in PEERS intervention affects parents and families of teenagers with ASD in terms of parenting efficacy, parenting stress, and family functioning.

*Methods:* Fifty parent-adolescent dyads (mean adolescent age = 13.7 years) were randomly assigned to an "Experimental" ($n$ = 23) or "Waitlist Control" ($n$= 27) group for PEERS intervention. Parents in both groups completed the Parenting Sense of Competency (PSOC) scale, a measure of family disruption (CHAOS scale: Matheny et al., 1996), and the Stress Index for Parents of Adolescents (SIPA) prior to and immediately following the Experimental group's participation in PEERS. Adolescents with ASD and their parents in the Experimental group then participated in 14 weeks of sessions focusing on initiating and maintaining friendships. Group-level analyses included bivariate correlations, paired samples t-tests, and mixed between-within subjects Analysis of Variance (ANOVA); Individual-level analyses included reliable change measures (Jacobson & Truax, 1991) for the SIPA.

*Results:* Bivariate correlations indicated a significant inverse relationship between parenting self-efficacy and total parenting stress, $r$ = -.473, $n$ = 50, $p$ = .001, and family disruption, $r$ = -.483, $n$ = 50, $p$ < .001, before PEERS. There was a significant increase in parenting self-efficacy from pre- to post-PEERS in the Experimental group, $t$ (22) = -2.18, $p$ = .04. There was a significant interaction between time and group for family disruption, $F$ (1, 48) = 5.61, $p$= .02, indicating a decrease over time in family disruption for the Experimental group compared to the Waitlist Control group. Finally, individual-level analyses indicated that 6 of 17 parents (who decreased in stress levels) demonstrated a reliable decrease in parenting stress.

*Conclusions:* Taken in sum, these results suggest that significant and positive changes occur in parents and families of adolescents with ASD following involvement in PEERS. Parents participating in PEERS experience decreased parenting stress and family disruption, and increased parenting efficacy, following the intervention, and are likely better able to help their adolescent as a result. In conjunction with previous literature on PEERS, this study highlights the overall efficacy of this intervention.

**105.006** Longitudinal Outcomes of Unstuck and on Target Executive Function Intervention Trial in Children with ASD. L. Kenworthy*[1], C. Luong Tran[1], K. M. Dudley[2], M. Werner[3], J. F. Strang[1], A. C. Armour[1], G. L. Wallace[4] and L. G. Anthony[1], (1)*Children's National Medical Center*, (2)*Children's National Medical Center*,, (3)*The Ivymount School*, (4)*National Institute of Mental Health*

Background:

Executive dysfunction is common in autism spectrum disorders (ASD) and is linked to academic, social and adaptive problems. Unaware of any contextually based executive function (EF) intervention for children with ASD without ID, we developed a school/home-based intervention targeting flexibility, goal-setting and planning called *Unstuck and On Target* (UOT). UOT remediates EF deficits in ASD through a cognitive/behavioral program that emphasizes self-regulatory scripts, guided/faded practice, and visual/verbal cueing in school and at home. We found that UOT improved flexibility, planning, and efficiency of problem solving even when compared to a social skills intervention of equal intensity in a randomized control trial (RCT). Whether improvements related to UOT are sustained beyond the duration of the intervention is unknown.

Objectives: To evaluate whether gains in flexibility, planning and problem solving attributed

to UOT are maintained 1 year after the completion of the intervention.

Methods:

Thirty-one (28 male, 18 White, mean age 11.4+0.96 years) of the 47 children with ASD who received UOT in an RCT were evaluated for follow-up 12-13 months after the completion of the intervention. All children had IQ>70 (mean=111+17), and met criteria for ASD on ADOS or ADI and clinician impression upon entrance into the RCT. The UOT intervention was delivered in school by school staff in small groups; classroom teachers and parents were trained to reinforce lessons. Results of the RCT indicated significantly greater pre-post improvement in the UOT participants than the comparison equal-intensity social skills intervention participants on the following measures: Wechsler Abbreviated Scale of Intelligence Block Design (BD) subtest; a play interview task posing flexibility and planning challenges called The Executive Function Challenge Task (EFCT; The EFCT yields Flexibility, Planning, and Social Appropriateness scores); parent ratings on the Behavior Rating Inventory of Executive Function (BRIEF) and the Flexibility Scale Interference score, which measures parent observed interference from inflexibility in daily activities. These measures were re-administered 12-13 months after the completion of the RCT and longitudinal post-intervention scores were compared to pre-intervention scores with paired sample *t* tests.

Results:

Benefit from UOT was maintained at longitudinal follow-up when compared to pre-intervention performance on the following measures: EFCT Planning, Flexibility and Social Appropriateness scores (*t's*>4.02,p's<.001); and parent BRIEF Shift (*t*=3.16,p=0.004) and Flexibility Questionnaire Interference (*t*=3.16,p=0.004) scores. Gains reported from pre- to post-UOT intervention on BD and parent BRIEF Plan/Organization were not sustained at a statistically significant level.

Conclusions:

One year following completion of the UOT intervention, gains in flexibility as observed in the laboratory and reported by parents were sustained. Gains in the area of planning and organization were also sustained as measured in the laboratory but not by parent report, and the improvement in efficiency of problem solving as assessed by the Wechsler Block Design subtest was not sustained. Replication of these data is required as the longitudinal follow-up data were collected under un-blinded conditions. These results are encouraging regarding the maintenance of flexibility skills learned in UOT and its on-going benefit in terms of reduced interference at home from inflexible behaviors.

**105.007** Personalized Cognitive Behavioral Therapy for Core Autism Symptoms in High Functioning Children. J. J. Wood*[1] and K. Sze Wood[2], (1)*University of California, Los Angeles*, (2)*UCLA*

Background: Cognitive behavioral therapy (CBT) is increasingly used in treating mood dysregulation in children with autism spectrum disorder, but to date, little evidence has accrued regarding the effects of CBT on core autism symptoms. This study compared personalized CBT with enhanced community care.

Objectives: To test whether CBT has a measureable impact on core autism symptoms as assessed by direct observational methods.

Methods: Twenty children with autism spectrum disorders (6-11 years old) were randomly assigned to 32 sessions of CBT or enhanced community care (ECC). The CBT program is based on the memory retrieval competition model and emphasizes the development of perspective-taking through guided behavioral experimentation supplemented with reflective Socratic discussion and supported by parent training and school consultation to promote generalization of social communication and emotion regulation skills. Trained observers blind to treatment condition observed each child at baseline and posttreatment, using the POPE, a structured behavioral observation system that generates frequency scores for observed social communication-related autism symptoms.

Results: CBT outperformed ECC at posttreatment on the primary observational outcome measure, quality of engagement state. At posttreatment, children in CBT exhibited less self-isolation, more time with peers, engaged more positively and appropriately with peers, and received more positive or appropriate peer responses than children in ECC, with a large effect size ($p < .05$).

Conclusions: CBT, when modified for children with ASD and targeted at core autism symptoms, may be beneficial for improving ASD-related social communication deficits. Data on the effects of CBT on other measures of ASD symptoms will further elucidate the extent of this positive effect.

**105.008** RCT of Mind Reading and in Vivo Rehearsal on the Emotion Encoding and Decoding of Children with High-Functioning ASDs. R. Smith*[1], M. L. Thomeer[2], C. Lopata[2] and M. A. Volker[1], (1)*University at Buffalo*, (2)*Canisius College Institute for Autism Research*

Background: Children with high-functioning ASD (HFASD) often exhibit deficits in encoding and decoding of emotions (e.g., Baron-Cohen et al., 1997; Volker et al., 2009) which may contribute to their clinical difficulties. Computer programs, such as *Mind Reading* (*MR*; Baron-Cohen et al., 2004) have been proposed to address the emotion-recognition deficits. Although *MR* studies have yielded preliminary support of efficacy for children with HFASD (e.g., LaCava et al., 2007), randomized trials of the software are needed that include larger samples, control groups, comprehensive assessment of treatment impact (proximal and distal measures), and evaluation of maintenance.

Objectives: This RCT evaluated the efficacy of *MR* and in vivo rehearsal on targeted emotion encoding and decoding skills (proximal measures), and broader decoding skills, autism symptoms, and social skills (distal measures) of children with HFASD.

Methods: *Participants:* Forty-three children, ages 8-12 with HFASD met inclusion criteria (short-form IQ >70; language score >80; and ADI-R score meeting ASD criteria) and were randomly assigned to either the treatment or wait-list control. *Proximal outcome measures: Cambridge Mindreading Face-Voice Battery for Children* (CAM-C Faces and Voices subscales) and *Emotion Recognition and Display Survey* (ERDS Receptive and Expressive subscales). *Distal outcome measures: Diagnostic Assessment of Nonverbal Accuracy2* (DANVA2 Adult Faces and Child Faces subscales), *Social Responsiveness Scale* (SRS), and *Behavior Assessment System for Children-Second Edition-Parent Rating Scale* (BASC-2 PRS; Social Skills subscale). Participants were assessed at pretest, posttest, and 5 weeks following treatment. *Procedures:* The manualized *MR* and in-vivo rehearsal protocol was administered during 24 staff-supervised 90-minute sessions. Children completed *MR* exercises (Emotions Library, Learning Center, etc.) and in vivo rehearsal according to a manualized protocol. Children earned *MR* generated computer-based rewards, and earned points for identifying and displaying emotions and following program and social rules.

Results: *Proximal measures:* Significant between-condition omnibus *F* results were examined using Bonferroni-corrected *post hoc* comparisons of posttest and follow-up scores (controlling for pretest). Results indicated significantly better emotion decoding of faces and voices taught in *MR* (CAM-C) and encoding of targeted emotions (ERDS Expressive) for the treatment group (vs. controls) at posttest and follow-up. Parent ratings of decoding (ERDS Receptive) were non-significant at posttest but significant at follow-up (favoring the treatment group). *Distal measures:* Significant between-condition omnibus *F* results were examined using uncorrected *post hoc* comparisons of posttest and follow-up scores (controlling for pretest). Results indicated significantly better decoding of emotions in children's faces not directly taught (DANVA2 Child Faces) at posttest for the treatment group; this was not maintained at follow-up. The treatment group also received significantly lower ratings of ASD symptoms at posttest and follow-up versus controls. Results were non-significant for the DANVA2 Adult Faces and BASC-2 Social Skills subscales.

Conclusions: Children who used *MR* learned to identify emotions in faces and voices directly taught in the program, and exhibited some degree of skill generalization to stimuli not directly taught. They also exhibited significant improvements in parent-rated expressions of emotions and significant decreases in ASD symptoms. Broader social skills were not significantly impacted, suggesting the need for enhancement of the protocol.

## 106 Early Development

**106.001 1** "Non Invasive Tools for Early Detection of Autism Spectrum Disorders". M. L. Scattoni*[1], A. Guzzetta[2], F. Apicella[3], M. Molteni[4], C. Manfredi[5], G. Pioggia[6], P. Venuti[7], R. Canitano[8], G. Tortorella[9], G. Vallortigara[7], G. Valeri[10], S. Vicari[11], F. Muratori[12] and A. M. Persico[13], (1)*Istituto Superiore di Sanità*, (2)*Stella Maris Institute*, (3)*"Fondazione Stella Maris" Scientific Institute*, (4)*'Eugenio Medea' Scientific*

*Institute*, (5)*Università degli Studi di Firenze*, (6)*National Research Council of Italy (CNR)*, (7)*University of Trento*, (8)*University hospital of Siena*, (9)*Universita' di Messina*, (10)*Children Hospital Bambino Gesù - Roma*, (11)*Child Neuropsychiatry Unit, "Children's Hospital Bambino Gesù"*, (12)*Stella Maris Scientific Institute*, (13)*University Campus Bio-Medico*

Background: Autism spectrum disorders (ASDs) are often not diagnosed until children reach 3-4 years of age. So far, the study of the early symptoms of ASDs is mainly based on retrospective analysis of home videotapes, usually recorded during children's first birthday party, or prospective studies of infant siblings of children with ASDs using the Autism Observation Scale for Infants, which measures visual attention, response to name, social babbling, eye contact and sensory behaviors. Neither home video analysis nor high risk infants studies, detected consistent abnormalities before 1 year of age. Early identification of young children with ASDs, possibly through a set of behavioral and neurophysiological indexes, is crucial in light of findings indicating that early intervention is much more effective than interventions starting in later childhood.

Objectives: Aim of our study is to identify early diagnostic markers through the assessment of neurobiological and developmental patterns in infant siblings of children with ASDs. We focused on age-specific motor (general movements analysis) and vocal repertoires (infant crying analysis), which are known to be later impaired in ASD children and that have been found altered in other neurodevelopmental disorders. General movements and cry analyses are of great relevance since they provide information concerning both development and integrity of the central nervous system and are completely non-invasive and easy to perform.

Methods: Recruiting of full term infants without genetic/neurological abnormalities and younger siblings of children diagnosed with ASDs; assessment of normative values for vocal, motor parameters and neuropsychological markers. Infant spontaneous movements and crying will be video- and audio-recorded at home in presence of a primary caregiver in the first six months of age. Subsequently, their neuropsychological and language development will be evaluated (AOSI, ADOS-T, Griffiths Mental Developmental Scales-ER; Peabody Motor Development Scale; MacArthur and First Year Inventory).

Results: So far, we recruited 80 full term infants and 14 high risk infants. Analysis of infant crying revealed that high risk infants have a lower frequency of fundamental frequency and of the two resonance frequencies F1 and F2 as compared to full term subjects. General movements analysis, an effective tool in predicting abnormal outcome in infants at risk for neurological development, revealed an unusual motor pattern in infants at high risk. Specifically, only 5 out of 14 high risk infants reached the maximum motor optimality score during the writhing movement period (10 days and 6 weeks) and 7 out of 14 infants during the fidgety period (12 weeks). Five high risk infants showed no responses to name, deficits in emotion recognition, and poor motor development.

Conclusions: Our preliminary results showed the importance of monitoring high-risk infant development during the first six months of life and suggest the usefulness of these non-invasive tools to identify early diagnostic markers. However, the sample size, primarily of high risk subjects, needs to be increased.

**106.002 2** How Do Early ASD Screening Scores Relate with Motor and Language Development in a Community Sample?. A. Ben-Sasson*[1] and S. V. Gill[2], (1)*University of Haifa*, (2)*Boston University*

**Background:** Early screening for autism spectrum disorders (ASD) has been primarily studied in high risk populations. Less is known about the validity of such tools in low-risk infants and their correspondence with developmental discontinuity (i.e. increase or decrease beyond normative expectations). Different types of markers may assist in identifying infants with different developmental needs.

**Objectives:** To determine the association of ASD risk on a parent questionnaire at 12-months with (1) concurrent developmental status, as well as with (2) increase or decrease in specific developmental areas from 13 to 30 months.

**Methods:** Seventy-six infants (55% boys) had the First Year Inventory (FYI) completed by their parents at 12 months. The FYI consists of a social-communication risk score and a sensory-regulatory risk score. The Mullen Scales of Early

Learning (MSEL) was administered at 13- and 30-months. Toddlers were classified as stable, increasing, or decreasing by at least 1.5 standard deviations (SD) on their developmental quotient (DQ) scores in each of the five MSEL areas from 13 to 30 months. Between 3.9%-51.3% of the sample was classified as increasing, and 0-23.7% as decreasing across areas.

**Results:** Of those with decreasing scores in the Gross Motor, Fine Motor and Expressive Language areas 22%, 19%, and 25% respectively had a developmental diagnosis at 30 months including ASD. There was not a higher rate of children with FYI risk in the decreasing versus stable and increasing groups. Higher FYI social-communication risk scores were associated with lower MSEL DQ scores at 13 months (Gross Motor $r(76)=-.20$, $p=.08$; Fine Motor $r(76)=-.30$, $p=.01$; Visual Perception $r(76)=-.28$, $p=.02$; Receptive Language $r(76)=-.58$, $p<.001$; Expressive Language $r(76)=-.43$, $p<.001$) and at 30 months (Gross Motor $r(76)=-.40$, <.001; Receptive Language $r(76)=-.33$, $p<.001$; Expressive Language $r(76)=-.38$, $p<.001$). The FYI sensory-regulatory risk score was not associated with MSEL scores at 13 months and modestly correlated with Receptive Language at 30 months, $r(76)=-.23$, $p=.03$.

FYI social-communication and sensory-regulatory scores were compared between the MSEL difference groups. Of all MSEL area difference groups, independent sample t-tests showed that children in the *Gross Motor* decreasing group had significantly higher sensory-regulatory risk scores than children in the stable group ($M=19.51$, $SD=10.79$, $M=13.13$, $SD= 9.24$ respectively, $t(70)=-2.43$, $p=.02$, $d=0.64$). For *Receptive Language,* children in the increasing group had significantly lower risk on the sensory-regulatory domain than in the stable group ($M=12.33$, $SD=9.55$, $M=17.32$, $SD= 9.61$ respectively, $t(74)=2.27$, $p=.03$, $d=0.52$).

**Conclusions:** A decrease in developmental status beyond normative expectations was not necessarily an 'alarming' signal. FYI social-communication risk was associated with developmental status at each age but did not explain change over 18 months. Elevated sensory-regulatory risk characterized infants who showed a decrease in their gross motor skills while reduced risk in this area characterized infants who increased in their receptive language. Sensory-regulatory risk status may play a pivotal role in shaping developmental change.

**106.003 3** Individual Behavioural Profiles and Predictors of Outcomes to the Early Start Denver Model Intervention. L. Ruta*[1], F. Muratori[1], M. Boncoddo[2], V. Cigala[3], C. Colombi[4], F. I. Fama'[5], A. Narzisi[6], R. Siracusano[7], G. Pioggia[7] and G. Tortorella[8], (1)*Stella Maris Scientific Institute*, (2)*Institute of Clinical Physiology, National Council of Research*, (3)*National Research Council of Italy*, (4)*University of Michigan*, (5)*Institute of Clinical Physiology, National Research Council of Italy*, (6)*Division of Child Neurology and Psychiatry, Stella Maris Scientific Institute, Pisa, Italy*, (7)*National Research Council of Italy (CNR)*, (8)*Universita' di Messina*

Background: Differential responsiveness to intervention programs in toddlers and pre-schoolers with Autism Spectrum Disorders (ASD) might be related to several factors, including pre-treatment cognitive and adaptive skills, communication abilities and individual behavioural characteristics.

Objectives: to investigate (i) factors associated with treatment effectiveness and (ii) behavioural profiles associated with response to the Early Start Denver Model (ESDM) intervention.

Methods: 20 ASD toddlers and pre-schoolers, aged 18-44 months participated in the "Prima Pietra" Project at the Pervasive Healthcare Centre (PHC), National Research Council of Italy, Messina, where an ESDM based intervention in which therapists were learning the model ("Learning ESDM" treatment) was applied. Children received between 5 to 10 hrs of treatment per week. Diagnostic assessment at baseline and after 3 months of treatment comprised the Autism Diagnostic Observation Schedule (ADOS), the Griffiths Mental Development Scale (GMDS), the *Vineland Adaptive Behaviour Scale (VABS),* the MacArthur Communicative Development Inventory and the Social Communication Questionnaire. The child's behavioural profile was assessed using the Child Behaviour Checklist 1½–5 (CBCL 1½–5). The correlations between putative predictors and outcome measures (in terms of change scores between pre- and post-treatment) after 3 months of treatment were analyzed and a linear regression on those predictors that showed a significant correlation with the outcome measures was performed.

Results: Baseline receptive language was positively correlated with and predicted gains in the general developmental quotient (GDQ) and gains in the personal-social skills and language were positively correlated with emotional reactivity and anxiety problems at baseline. Furthermore, aggressive behaviours were negatively correlated with ADOS scores at baseline and predicted a lower gain in personal-social skills after 3 months of treatment.

Conclusions: Our results suggest that individual behavioural profiles and receptive language abilities at baseline correlate with and predict outcomes at 3 months of an ESDM treatment.

**106.004 4** The Expressive Vocabulary Profile in Young Children with Autism Spectrum Disorder. T. L. Lin*[1], C. H. Chiang[1], C. L. Chu[2] and C. C. Wu[3], (1)*National Chengchi University*, (2)*National Chung Cheng University*, (3)*Department of Psychology, Kaohsiung Medical University*

**Background**: Autism spectrum disorder (ASD) is characterized by qualitatively impairments in social reciprocity and communication, and manifested repetitive and stereotyped behaviors/interests, with onset during early childhood. Parents of ASD often found out something wrong with their children since they didn't say any or few words around 2-year-old. After being diagnosed with ASD and having interventions, some children can develop their language gradually.

**Objectives**: The purpose of this study was to examine the developmental profile of expressive vocabularies in young children with ASD.

**Methods**: Seventy five children diagnosed with ASD between 24 and 58 months of age (at mean age of 40 months) were recruited and divided into two groups: children with higher nonverbal developmental quotient (NVDQ > 80) and children with lower NVDQ (NVDQ < 80). Mandarin-Chinese Communicative Development Inventory (Taiwan) (MCDI-T) was used to measure the development of expressive vocabularies.

**Results**: Children with higher NVDQ expressed significantly more vocabularies in all 19 categories in MCDI-T than children with lower NVDQ. However, the two groups had the similar profile of expressive vocabulary composition: expressing the lowest proportion in connecting words, and the order of top three categories were action words, food/drink and people. When the 19 categories were reduced into four categories (social terms, common nouns, predicates and grammatical function words), the two groups also had the similar profile: the highest proportion in common nouns and the lowest proportion in grammatical function words.

**Conclusions**: This study manifests that NVDQ is highly correlated with the expressive vocabulary size. However, since children with ASD began to expressive vocabularies, they have the same expressive profile, regardless of NVDQ, with typically developing children according to other previous studies. The future studies should include comparison groups, such as children with typical development and developmental delay, to further clarify the expressive vocabulary profile in young children with ASD.

**106.005 5** A Comparison of the BASC-2 Preschool Version in Toddlers and Preschool Children with ASD and Other Developmental Delays. L. E. Bradstreet*[1], J. Juechter[2], R. W. Kamphaus[1] and D. Robins[1], (1)*Georgia State University*, (2)*Bigfork Public Schools*

**Background:** The Behavioral Assessment System for Children, Second Edition (BASC-2), is a comprehensive rating system that identifies adaptive and maladaptive patterns of behavior in youth between the ages of 2-21 years. A number of studies have examined the utility of score profiles on clinical (e.g., Anxiety, Atypicality) and adaptive (e.g., Social Skills, Adaptability) scales on the BASC-2 Parent Rating Scales (PRS) for identifying school-aged children with autism spectrum disorder (ASD). However, few studies have examined the utility of broad behavioral measures for differentiating toddlers and preschool children with ASD from youth with other developmental delays.

**Objectives:** The purpose of this project is to test the hypothesis that the BASC-2 Preschool clinical and adaptive scales will differentiate toddlers and preschool children with ASD from youth with other developmental delays.

**Methods:** As part of a larger test battery, BASC-2 Preschool PRS were completed by the primary caregivers of 120 youth 24-61 months old ($M$ = 34.78, $SD$= 9.54) referred for evaluation after they screened positive on an ASD screener (M-CHAT-R) or caregivers and/or pediatricians raised concerns regarding ASD. Of those children, 82

were diagnosed with ASD and 38 were diagnosed with other developmental delays (Other DD). Diagnoses for individuals with ASD were confirmed by expert clinicians using the Autism Diagnostic Observation Schedule and structured parent interviews. Two multivariate analyses of covariance (MANCOVAs) were run to determine if scores on the clinical and adaptive scales of the BASC-2 differed between groups, including age as a covariate.

**Results:** No significant differences were found between the ASD group and the Other DD group in regard to sex $\chi^2$ (1, $N$=120) = 1.93, $p$>.05 or ethnicity $\chi^2$ (1, $N$=117) = .01, $p$>.05. The ASD group received significantly higher scores on the clinical scales than the Other DD group, $F$ (8, 110) = 3.53, $p$<.001, Wilk's Λ = .80, $\eta^2$= .20. Post-hoc individual ANCOVAs revealed that the ASD group had significantly higher scores than the Other DD group on the Attention Problems ($F$ [1, 117] = 9.05, $p$=.003), Atypicality ($F$ [1, 117] = 6.08, $p$=.015), and Withdrawal ($F$ [1, 117] = 14.59, $p$<.001) scales. There were no significant differences between the ASD group and the Other DD group on adaptive scales, $F$ (4, 113) = 1.92, $p$>.05, Wilk's Λ = .94.

**Conclusions:** The present data indicate that toddlers and preschool children with ASD may demonstrate distinct patterns of clinical behaviors on the BASC-2 compared to youth with other developmental delays. Specifically, youth with ASD were rated as having more challenging behaviors on the Attention Problems, Atypicality, and Withdrawal scales. These results suggest that young children with ASD may be at a greater risk for certain behavioral difficulties compared to youth with other developmental delays; this supports previous research examining the emergence of challenging behaviors in youth with ASD and other developmental delays. Early interventions for youth with ASD may be able to target these challenging behaviors and in turn reduce or prevent the continuation of these behaviors by the time the children enter the school system.

**106.006 6** A Prospective Study of Toddlers with ASD: A Short-Term Diagnostic Stability and Developmental Outcome. C. H. Chiang*[1], C. L. Chu[2], C. C. Wu[3], Y. M. Hou[4] and J. H. Liu[5], (1)*National Chengchi University*, (2)*National Chung Cheng University*, (3)*Department of Psychology, Kaohsiung Medical University*, (4)*Chia-Yi Christian Hospital*, (5)*Liouying, Chi Mei Medical Center*

Background: Recent literature demonstrated that the number of toddlers referred for a differential diagnosis of autism spectrum disorders (ASD), short-term stability of the early diagnosis in this cohort lack in Taiwan.

Objectives: The purpose of the study was to report the diagnostic stability and the developmental outcomes in the children with ASD at age 2 as Time 1 and followed them at age 4 in Taiwan.

Methods: Eighty-six children were diagnosed with ASD (n = 44) or developmental disorder (DD)(n = 42) between 24 and 36 months (Time 1, mean = 28.97 months, SD = 4.1 months) and re-diagnosed between 42 and 55 months (Time 2, mean = 47.53 months, SD = 4.2 months). Diagnoses based on clinical judgment using DSM-IV and Autism Diagnostic Observation Scales (ADOS, Lord, et al, 1999) in Time 1 and added Autism Diagnostic Interview-Revised (ADI-R, Lord, et al, 1994) at time 2.

Results: First, according to clinical judgment, the consistency between two time point in autistic disorder (AD), pervasive developmental disorder-NOS (PDDNOS) and DD were 78.9%, 44.4% and 89.7%, respectively. Regarding ADOS diagnosis at two time point, the consistency in AD, PDDNOS, and DD were 71.3%, 31.2% and 91.4%, respectively. At time 1, the consistency between clinical judgment and ADOS in AD, PDDNOS and DD were 92.3%, 54.1% and 94.2%, respectively. At time 2, the steadiness between clinical judgment and ADOS in AD, PDDNOS and DD were 94.6%, 70.5% and 95.2%, respectively. While using ASD and non-ASD as categorization, the consistency between clinical judgment and ADOS were 95.4% and 84.6% at time 1, and 95.4% and 97.6% at time 2 respectively. Second, at time 1, the proportions of DQ>70 in the children with AD, PDD-NOS and DD were 28.6%, 44.4% and 54.8% respectively. However, the rate of DQ>70 in the children with AD, PDD-NOS and DD were generally increased to 47.6%, 56.1% and 61.8%. The type and duration of early intervention were associated with the developmental outcome.

Conclusions: Stability of early diagnosis in ASD indicated an acceptable level at age 2 and more consistent at age 4 based on DSM-IV. The quality

and quantity of early intervention were related to the cognitive outcome. Future studies should use DSM-5 for exploring the issue in diagnostic stability and developmental outcome.

**106.007 7** ASD Screening at 18 and 24 Months: Incremental Validity and Characteristics of Screen Positive Cases. C. Chlebowski*[1], D. A. Fein[2] and D. Robins[3], (1)*University of California, San Diego*, (2)*University of Connecticut*, (3)*Georgia State University*

Background: The American Academy of Pediatrics has recommended autism screening for all children at 18 and 24 months, but empirical data are lacking to determine the added value of screening at two time points.

Objectives: To investigate the incremental validity of a second screen at 24 months and compare children who screened positive on a second autism screening at 24 months to children who screened positive at 24 months without a previous autism screen.

Methods: The 2-stage M-CHAT with Follow-Up (M-CHAT/F) was used to screen children at 18 and 24 month pediatric well child visits; screen positive cases were evaluated and classified with an Autism Spectrum Disorder (ASD) or non-ASD. Participants in the current study include children who screened positive at 24-months.

Results: Of 7,364 children screened with M-CHAT at both 18 and 24 months, 32 children screened negative on the M-CHAT(/F) at 18 months and screened positive on the M-CHAT/F at 24 months. The sample was majority male (59.4%) and represented a range of races/ethnicities (34.4% White, 34.4% African American, 12.5% Hispanic/Latino). Of the 32 cases, 9 families declined the diagnostic evaluation. Of the 23 children who received evaluations, 11 children were diagnosed with an ASD (5 Autistic Disorder, 6 PDD-NOS), 9 children received other DSM-IV or ICD-10 diagnoses, 2 children were classified as "at risk" with developmental concerns, and one child was typically developing.

All children who screened positive with a second autism screening at 24 months (n=23) were compared to children who screened positive at 24 months without a previous autism screen (n=145). There were no differences between the samples in regards to autism symptoms or severity as measured by the ADOS total score ($t$=-.636, $p$=.526) or the CARS total score ($t$=-.901, $p$=.369). When comparing cognitive functioning as measured by the Mullen Scales of Early Learning (MSEL), there were no differences between the two groups in receptive or expressive language skills. There was a trend towards significance on the MSEL Fine Motor domain ($t$=1.921, $p$=.056) and a significant difference on the MSEL Visual Reception domain ($t$=2.096, $p$=.038). The children who were identified with a second autism screening at 24 months had higher t-scores on both the Fine Motor (32.4 vs. 27.9) and Visual Reception (36.9 vs. 31.1) domains.

Conclusions: Completing a second autism screening at 24 months identified 11 additional cases of ASD. There were no significant differences between children who screened positive on a second autism screening as compared to children who screened positive without a previous autism screen, with the exception of performance on the MSEL Visual Reception domain. Additional investigation is needed to identify potential differences between the samples, which might help identify children who are likely to be "missed" by an autism screen at 18 months.

**106.008 8** Accommodations Made By Parents Raising Children with Autism Spectrum Disorder. T. Soto*[1], N. D. Slade[2], A. Eisenhower[1] and A. S. Carter[2], (1)*University of Massachusetts, Boston*, (2)*University of Massachusetts Boston*

Background: The stress associated with raising a child on the autism spectrum is well documented (e.g., Gray, 1994, 2002; Hutton & Caron, 2005). Parents of children with ASD experience higher levels of stress than parents of children who are typically developing (Rao & Beidel, 2009) and seem to experience more stress than parents of children with other types of disabilities as well (e.g., Blacher & McIntyre, 2006). Moreover, parental stress has been associated with a lack of social support and effective coping strategies (e.g., Weiss, 2002); parent depression (e.g., Montes & Halterman, 2008); the severity of children's autism symptoms (Osborne, McHugh, Saunders, & Reed, 2008), and child behavior problems (e.g., Levavalier, Leone, & Wiltz, 2006). However, there has been limited research documenting the association between characteristics of children with ASD and family accommodations, or the manner in which parents modify daily routines in response to a child's

special needs. Identifying the accommodations made by parents raising a child with ASD will help inform parent-mediated interventions and will ultimately promote healthier family functioning.

Objectives: (1) document the rates and cost/benefit ratio of accommodations made by parents of children with ASD across five factors of accommodations – employment, finances, social activities, family communication, and religious activities; and (2) investigate parent and child characteristics that predict the rates and cost/benefit ratio of accommodations made by parents of children with ASD.

Methods: As part of a larger study, mothers (n = 174) of young children with ASD (n = 174; between 18 and 33 months of age) were asked question during a structured interview about making accommodations due to their child's needs in six domains. Parents were also asked to rate how costly or beneficial the accommodations were to their family on a five-point scale. The Infant Toddler Social and Emotional Assessment (ITSEA) was used to assess child dysregulation symptoms; the Toddler Behavior Assessment Questionnaire (TBAQ) was used to inhibitory control. The Parenting Stress Index-Short Form (PSI-SF) was used to assess parenting stress.

Results: Two hierarchical multiple linear regression models were used to test the relation between child dysregulation symptoms, parenting stress and accommodations made by parents. In the first model ($F$=8.87, p<.001), when entered together PSI [(ß = .265), p < .01] accounted for unique variance in the total number of accommodations made by parents, whereas ITSEA Dysregulation [(ß = .204), P<.01] accounted for unique variance only when entered separately. In the second model ($F$=16.2, p<.001), TBAQ Inhibitory Control (ß = -.28, p<.001) and PSI (ß=-.25, p<.01) each accounted for unique variance in Total Cost/Benefit of accommodations made by parents.

Conclusions: Results indicate that parent stress level and child inhibitory control predict the presence and severity of family accommodations. These results add to the limited body of research examining accommodations made by parents raising children with ASD and suggest that family support is an important factor in early intervention for children with ASD.

**106.009 9** Adaptive Skills in Toddlers with DSM-IV but Not DSM-5 Autism. D. T. Jashar*[1], L. A. Brennan[1], D. Robins[2], M. L. Barton[1] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Georgia State University*

Background:

The DSM-5 diagnostic criteria for Autism Spectrum Disorders (ASD) has raised concerns about diagnostic sensitivity for very young children (Worley & Matson, 2012). One main concern is that children with marked social and communication difficulties who met ASD criteria on DSM-IV-TR may fail to meet the DSM-5 diagnostic criteria, especially on the restrictive and repetitive behaviors subdomain (RRB's) (Gibbs et al., 2012; Barton et al., 2013). Though these individuals are impaired in social and communication functioning, it is unclear how they are different and/or similar to those who retain their diagnosis.

Objectives:

In a previous study, we examined whether toddlers who received an ASD diagnosis under the DSM-IV-TR criteria would maintain their diagnosis using DSM-5 criteria. The results (reported at IMFAR 2013) indicated that 29% of toddlers who previously met an ASD diagnosis no longer did so with the new criteria. The current study examined the parent-reported adaptive functioning of toddlers with an ASD diagnosis under DSM-IV-TR but not with DSM-5 (DSM-IV-only group) and compared these scores to those of toddlers who retained the ASD diagnosis under DSM-5 criteria (DSM-5 group) and a comparison group of toddlers who were diagnosed with a Developmental Language Disorder (DLD group; Mixed Expressive/Receptive Language Disorder under the DSM-IV-TR).

Methods:

Parents of 37 children with DSM-IV-only ASD, 37 children with DSM-5 ASD (all of whom met for DSM-IV-TR), and 12 DLD participants between the ages of 18 and 34 months ($M$=25.25, $SD$=4.61) completed the Vineland Adaptive Behavior Scales Interview (Sparrow, Balla, & Cicchetti, 1984), which assesses skills in the Communication (expressive and receptive language subdomains), Daily Living Skills (personal, domestic, community subdomains), Socialization (interpersonal, play and leisure, coping subdomains), and Motor

domains (gross, fine subdomains). The adaptive level, which is a descriptive category for each subscale, was analyzed (i.e., 1=low, 2=moderately low, 3=adequate, 4=moderately high, 5=high).

Results:

Descriptive statistics, ANOVA, and t-tests were conducted to determine whether the subdomain scores differed by group.

Results indicated that the DSM-IV-only ASD group scored significantly higher than the DSM-5 ASD group in the expressive language ($t(72)=2.51$, $p=.01$), receptive language ($t(72)=4.15$, $p=.00$), personal ($t(72)=2.78$, $p=.01$), interpersonal ($t(72)=2.63$, $p=.01$), and play and leisure ($t(72)=2.85$, $p=.01$) subdomains. The DSM-IV-only group scored significantly lower than the DLD group in the play and leisure ($t(47)=-3.43$, $p=.00$), and fine motor ($t(47)=-2.67$, $p=.01$) and gross motor ($t(47)=-2.65$, $p=.01$ subdomains. The DSM-5 group scored significantly lower than the DLD group in all subdomains except domestic and coping skills.

Conclusions:

Although both ASD groups were lower functioning than the DLD children on most adaptive domains, the toddlers in the DSM-IV-only ASD group were less developmentally delayed in their adaptive skills than the children who continue to meet ASD criteria in DSM-5. It is of concern that the DSM-IV-only group, which might have the most potential for good outcomes because of smaller developmental delays, might not be able to get effective autism-specific services without an ASD diagnosis.

**106.010 10** African American Toddlers with ASD Demonstrate More Social-Communication Symptoms Than Caucasian Toddlers.

B. Brooks*[1], L. E. Herlihy[2] and D. Robins[1], (1)*Georgia State University*, (2)*University of Connecticut*

**Background:** Understanding differences in symptom presentation across racial groups may be helpful in reducing disparities in the early identification of autism spectrum disorder (ASD). Given that African American (AA) children are typically misdiagnosed or diagnosed later than their Caucasian (CA) peers, it is necessary to explore differences in the direct observation of autism-specific symptoms.

**Objectives:** This exploratory study investigated differences in direct observations of social-communication symptoms in toddlers at risk for ASD. Racial differences will be explored while controlling for socioeconomic status, as measured by maternal education.

**Methods:** Parents completed the M-CHAT(-R) at pediatric 18- or 24-month well-child visits. Children at-risk based on the M-CHAT(-R)+Follow-up or a play-based screening measure, or whose parents/pediatrician expressed concerns about ASD were invited to complete a diagnostic evaluation ($N=195$,$M$age=26.56 months, $SD=5.13$). Evaluations included measures of ASD symptomatology (Autism Diagnostic Observation Schedule Module 1-ADOS), developmental level, and adaptive abilities. For the purpose of this investigation, children who received a diagnosis of developmental delay or developmental language disorder (non-ASD group), and ASD were included in the analyses. Typically developing children and those missing race and income data were excluded.

**Results:** Caucasian (CA; $N=102$; $M=15.51$ years, $SD=2.67$) mothers had significantly greater years of education than AA parents (AA; $N=74$; $M=13.60$ years, $SD=2.45$), $t=5.19$, $p<.001$. A series of 2x2 between-subjects ANOVAs examined race and diagnosis ($N_{ASD}=106$, $N_{non\text{-}ASD}=70$), controlling for maternal education. Results indicated a significant main effect of race on ADOS Communication, $F(1, 195)=7.41$, $p=.007$ and Play, $F(1, 195)=9.55$, $p=.002$. AA toddlers demonstrated greater communication ($M_{AA}=4.09$, $SD=1.92$ > $M_{CA}=3.42$, $SD=1.87$) and play deficits than CA toddlers ($M_{AA}=2.93$, $SD=1.17$ > $M_{CA}=2.56$, $SD=1.12$). There was also a significant race x diagnosis interaction for ADOS Social Interaction, $F(1, 195)=4.20$, p=.04. Within non-ASD, AA toddlers displayed fewer social symptoms than their CA peers ($M_{AA}=2.97$, $SD=2.59$ < $M_{CA}=3.57$, $SD=2.54$). In contrast, within ASD, AA toddlers displayed more social symptoms than CA toddlers ($M_{AA}=9.91$, $SD=2.92$ > $M_{CA}=8.90$, $SD=2.34$). There were no significant racial differences in the restricted/repetitive behaviors or ADOS comparison scores.

**Conclusions**: These findings suggest that under direct testing conditions AA toddlers may display weaknesses in their communication skills and pretend play. Additionally, AA toddlers with ASD

may display more social deficits (e.g., poor eye contact, reduced giving and showing) than CA toddlers with ASD. It is possible that AA toddlers may need to demonstrate more severe social deficits to receive a diagnosis from evaluators. Although maternal education was controlled for in these analyses, unmeasured factors related to SES, such as toys available in the home, exposure to other children, and experience in childcare were not investigated. For example, some children may be encouraged to sit and play quietly as opposed to being encouraged to play pretend. These factors may also have influenced toddlers' play and social skills during the observation. Future studies would benefit from exploring how cultural differences in the emphasis of pretend play and other aspects of social communication play a role in the assessment of early ASD symptomatology.

**106.011 11** Association Between Brain Function Measures and Parent-Child Interactions in the Autism Phenotype. M. Elsabbagh*[1], M. W. Wan[2], R. Bruno[3], J. Green[2], T. Charman[4], M. H. Johnson[5] and .. The BASIS Team[6], (1)*McGill University*, (2)*University of Manchester*, (3)*McGill University Health Centre - Research Institute*, (4)*King's College London*, (5)*Birkbeck College, University of London*, (6)*Birkbeck, University of London*

Background: Evidence suggests that autism emerges in toddlerhood as a result of early subtle differences in brain function within the first year that become compounded and amplified due to atypical interactions within developing brain systems and with the external environment (Elsabbagh and Johnson, 2010). Such dynamic and complex developmental pathways are difficult to test empirically. One approach is to explore links between brain function measures collected under controlled laboratory conditions and more naturalistic measures such as of parent-child interactions. Such associations may help clarify how atypical development of brain systems manifest at the behavioral level.

Objectives: We explored links between brain function measures in response to gaze stimuli and patterns of parent-child interactions in a group of 104 infants with and without a family history of autism in the first year of life.

Methods: Participants were drawn from the British Autism Study of Infant Siblings (BASIS) and included 104 families recruited sequentially into the study. Within this group, there were 54 at-risk infants (21 male, 33 female) and 50 control infants (21 male, 29 female). The infants were on average 7-months at the time of the study (*mean* = 238.3 days, *SD*= 37.2). Approximately 30% of the infants in the at-risk group received an autism diagnosis as toddlers. Data from two tasks were used for the current study. In the first task, ERPs were recorder while infants were seated on their parents' lap and facing a computer screen on which were images of female faces with gaze directed either towards or away from the infant. The second task was a Parent-child interaction (PCI) assessment, where a 6-min episode of unstructured play was videotaped during which the parent-infant dyad was seated on a floor mat in a room with a small set of toys.

Results: After initial exploration of factor structure within each task using Principal Component Analysis, variables which explained most of the variance were retained from the ERP (P100 latency and P400 amplitude and latency) and PCI (Infant positive affect, attentiveness and liveliness; Parent sensitive responsiveness, and Dyadic mutuality) tasks. Our findings suggest an association between ERP responses to eye gaze and parent-infant interaction measures. In both groups, infants with more positive affect exhibit stronger differentiation to gaze stimuli. This association was observed with the earlier P100 waveform component in the control group but with the later P400 component in infants at-risk. These findings held across the entire group and were not driven by the subgroup of infants who developed autism in toddlerhood.

Conclusions: These findings suggest that variability in functional brain development is associated with infants' overt behavior when examined within naturalistic interaction contexts. The results are critical in paving the way for a better understanding of how infant laboratory measures may relate to overt behavior and how both can be combined in the context of predicting risk or clinical diagnosis in toddlerhood.

**106.012 12** Attentional Domains of Parent-Reported Infant Behaviors: Implications and Relations to Social Responsiveness and Risk for Autism. R. Stephens*[1], M. G. Sabatos-DeVito[1], J. S. Reznick[1], L. Turner-Brown[1], L. R. Watson[2], G. T. Baranek[1] and E. R. Crais[1], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*

Background: Numerous studies have documented the strong relationship between a child's early

attentional skills and a later diagnosis of autism, especially for behaviors of initiating (IJA) and responding to joint attention (RJA), and overfocused attention (OFA). These relations are especially relevant considering the attention network model and associated brain regions (Posner & Peterson, 1989), with significant research associating aberrant activity or connectivity among networks associated with attention in individuals with autism (e.g., Mundy & Newell, 2007). Many behavioral and neurological deficits can be observed in children at risk for autism during infancy. Baranek and colleagues (2003) developed the First Year Inventory (FYI) to flag 12-month-olds at risk for a diagnosis of autism. Although this measure has accurately identified children who receive a diagnosis of autism or other developmental disorder (Turner-Brown et al., 2012), there may be value in exploring additional ways of scoring the FYI that could be associated with later cognitive deficits associated with autism.

Objectives: The objective of this study was to explore FYI items that may be specific to constructs of attention that could be useful as identifiers of eventual risk of autism, and then to look at associations between these new constructs and the children's later scores on the Social Responsiveness Scale – Preschool version (Pine et al., 2006).

Methods: Through a comprehensive review of the literature on typical and atypical infant attention development, and considerations of statistical and theoretical validity, we operationalized three new constructs of attention from the FYI items: IJA, RJA and OFA. An extant database with FYIs (N=7823) was analyzed using the new constructs to determine strength of relations among items. For this study, the new domains were applied to data obtained from parents of 12-month-olds in the original FYI cohort (N=1305; Reznick et al., 2007). Regression analyses were used to measure association of the new constructs to later measures of autism severity (SRS-P) at age 3 for a subset of 699 cases (Turner-Brown et al., 2012).

Results: Cronbach's alpha analysis indicated good internal consistency (0.763, 0.723, and 0.699 for IJA, RJA & OFA, respectively). Preliminary data analyses showed statistically significant relations between the scores on these domains at 12 months and SRS-P scores at age three ($R^2$=.15; $p < 0.01$ for all three variables).

Conclusions: Scores on three new attention-based constructs developed from the FYI items at 12 months of age were found to be significantly related to SRS-P scores at 3 years of age and support the notion that early attention skills may be associated with symptoms of autism. Scores on these three constructs may allow for the establishment of profiles of attention that could be used in longitudinal studies to better understand developmental trajectories for children at risk for ASD.

**106.013 13** Automated Prediction of a Child's Response to Name from Audio and Video. J. Bidwell*, A. Rozga, J. C. Kim, H. Rao, M. A. Clements, I. Essa and G. D. Abowd, *Georgia Institute of Technology*

Background: Evidence has shown that a child's failure to respond to name is an early warning sign for autism and is measured as a part of standard assessments e.g. ADOS [1,2].

Objectives: Build a fully automated system for measuring a child's response to his or her name being called given video and recorded audio during a social interaction. Here our initial goal is to enable this measurement in a naturalistic setting with the long term goal of eventually obtaining finer gain behavior measurements such as child response time latency between a name call and a response.

Methods: We recorded 40 social interactions between an examiner and children (ages 15-24 months). 6 of our 40 child participants showed signs of developmental delay based on standardized parent report measures (M-CHAT, CSBS-ITC, CBCL language development survey). The child sat at a table with a toy to play with. The examiner wore a lapel microphone and called the child's name up to 3 times while standing to the right and slightly behind the child. These interactions were recorded with two cameras that we used in conjunction with the examiner's audio for predicting when the child responded. Name calls were measured by 1) detecting when an examiner called the child's name and 2) evaluating whether the child turned to make eye contact with the examiner. Examiner name calls were detected using a speech detection algorithm. Meanwhile the child's head turns were tracked using a pair of cameras which consisted of

overhead Kinect color and depth camera and a front facing color camera. These speech and head turn measurements were used to train a binary classifier for automatically predicting if and when a child responds to his or her name being called. The result is a system for predicting the child's response to his or her name being called automatically recorded audio and video of the session.

Results: The system was evaluated against human coding of the child's response to name from video. If the automated prediction fell within +/- 1 second of the human coded response then we recorded a match. Across our 40 sessions we had 56 name calls, 35 responses and 5 children that did not respond to name. Our software correctly predicted children's response to name with a precision of 90%, recall of 85%.

Conclusions: This work presents an automated system for predicting child response to name with the aim of benefiting existing clinical and research communities. In the future this could could be extended to a support wide range of use cases such as gathering data on children's response to name in naturalistic settings (e.g. pediatric waiting rooms, day care centers and the home) as well as providing psychologists with a second source of information during clinical assessments.

References:

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**106.014 14** Behavioral Differences Between High-Risk and Low-Risk Children with Autism. K. R. Bradbury*, T. Dumont-Mathieu, M. L. Barton and D. A. Fein, *University of Connecticut*

Background: Family studies indicate that the recurrence risk for Autism Spectrum Disorders (ASD) in subsequent children is approximately 10-20%, significantly higher than in the general population. There is also evidence of a broader autism phenotype of subclinical ASD symptomatology in some family members not affected with ASD. Recent studies have suggested that there may be distinct genetic mechanisms in multiplex and simplex families with ASD, which suggests the possibility of behavioral differences that result from these differing underlying mechanisms. Due to the low base rate of ASD, many current prospective studies use high-risk samples, such as younger siblings of affected children, to examine the early emergence of ASD symptomatology. However, there is little research on the degree to which high-risk samples are representative of the greater population with ASD. Few studies have looked at differences between children with ASD from multiplex and simplex families with regard to scores on the Autism Diagnostic Interview (ADI), with mixed results. The current study examines potential behavioral differences between high- and low-risk samples, with regard to severity of ASD symptoms, cognitive ability, and adaptive functioning.

Objectives: To examine behavioral differences between children with ASD from multiplex and simplex families.

Methods: Children were evaluated as a result of screening positive on an ASD screener, the M-CHAT or M-CHAT-R. ASD diagnoses were based on Autism Diagnostic Observation Schedule (ADOS) and Childhood Autism Rating Scale (CARS) scores, and clinical impression. The high-risk sample ($n$=31) was composed of children with ASD who had an older affected sibling, found through clinical services or research involving the older sibling. A second sample ($n$=31) of children diagnosed with ASD was drawn from a low-risk sample, screened at well-child pediatric visits. Groups were matched on age, gender, and maternal education. High- and low-risk sample mean scores were compared on several measures including the ADOS, CARS, Mullen Scales of Early Learning (Mullen), and Vineland Adaptive Behavior Scales-II (Vineland). T-tests were utilized to determine whether significant differences existed between groups.

Results: Samples were well matched on age ($M_{\text{Low-Risk}}$=23.52 months, $SD$=4.34; $M_{\text{High-Risk}}$=23.61, $SD$=4.23), gender, and maternal education, and did not differ significantly on ethnicity. No significant differences between the high- and low-risk children were seen with regard to severity of autism symptoms as measured by the CARS and ADOS. Similarly, no significant differences were observed on any domain of the Vineland or on the Visual Reception scale of the Mullen. However, the high-risk cases had significantly higher mean scores than the low-risk children on the Fine

Motor, Expressive Language, and Receptive Language scales of the Mullen.

Conclusions: Preliminary analyses suggest that high-risk children may be somewhat higher functioning, or less developmentally delayed, than children drawn from the low-risk sample, in their language and fine motor skills, although their autism symptomatology and non-verbal cognitive abilities did not differ significantly. These results suggest that some caution may be needed in generalizing cognitive or behavioral findings from younger siblings to the larger population of children with ASD. Case ascertainment differences must be considered as possibly contributing to group differences.

**106.015 15** Comparing Perceptuo-Motor and Communication Development Across at-Risk Infants Who Later Developed Autism, at-Risk Infants without Delays, and Typically Developing Infants. L. Tran*, S. Srinivasan, M. Kaur and A. N. Bhat, *University of Connecticut*

Background: Infants who later develop Autism Spectrum Disorders (ASDs) show early gross motor delays (Ozonoff et al., 2008; Bhat, Galloway, & Landa, 2009). The majority of the studies have used retrospective data or general developmental assessments such as the Mullen Scales of Early Learning (Landa & Garrett-Mayer, 2005). Our recent publication reported presence of gross motor delays at 6 months that correlated with language delays at 18 months (Bhat, Galloway, & Landa, 2012).

Objectives: In the current study, we examined the differences in perceptuo-motor and communication development between infants at risk for autism (AU sibs) and typically developing (TD) infants and related them to infants' future language, social, and motor outcomes at 24 months.

Methods: 16 TD infants and 16 AU sibs were observed longitudinally at 3, 6, 9, 12, and 15 months of age using the Mullen Scales of Early Learning (MSEL) and the Alberta Infant Motor Scale (AIMS). We have obtained future outcomes on developmental concerns and ASD diagnoses at 18 and 24 months.

Results: We will particularly report on differences between AU sibs who later developed "developmental delays and ASDs" versus those who did not based on 18- and 24-month outcomes. In terms of AIMS performance, 5 to 7 of the 9 AU sibs who developed delays or ASD diagnoses by 24 months of age, demonstrated motor delays (at or below the 25$^{th}$ percentile) at the 6- and 12-month visits. Such delays were not observed at other ages. In terms of the MSEL performance, all 9 infants who developed future delays or ASD diagnoses showed delays in at least one domain of the MSEL at 12 or 15 months based on their T-scores values. Specifically, 8 out of 9 AU sibs demonstrated gross or fine motor delays at 12- or 15-months and 5 out of 9 infants demonstrated both receptive and expressive language delays at 12- or 15-months.

Conclusions: While communication delay is a frequent early marker of ASDs, we also believe that impairments in gross and fine motor control are present in AU sibs who later develop ASDs. This may contribute to the motor challenges the at-risk infant faces during social interactions such as effective use of non-verbal communication with others. Hence, it is important to detect and treat early motor delays and use motor assessments as a window for early diagnosis of future autism-related impairments.

**106.016 16** Components of Limited Activity Monitoring in Toddlers and Children with ASD. F. Shic*[1], G. Chen[2], M. Perlmutter[1], E. B. Gisin[1], A. Dowd[3], E. B. Prince[1], L. Flink[1], S. Lansiquot[1], C. A. Wall[1], E. S. Kim[1], Q. Wang[1], S. Macari[1] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Christian Academy in Japan (CAJ)*, (3)*University of Texas at Austin*

Background: Our previous work with eye tracking has shown that 20 month old toddlers with ASD monitor the activities of others to a lesser extent than both developmentally delayed and typically developing peers. However, it is unclear whether the gaze cues of others, the presence of distractors, or motion cues were responsible for the differences between groups. Furthermore, it is unclear whether diminished activity monitoring is only present in the toddler years, resolving as the children grow older, or whether these deficits persist.

Objectives: To use eye tracking to examine activity monitoring in toddlers and children with ASD and to decompose factors that impact activity monitoring.

Methods: Toddlers with ASD (N=10; Age: M=23, SD=3 months) and typical development (TD;

N=23; Age: M=21, SD=3 months) and children with ASD (N=17; Age: M=37, SD=1 month) and TD (N=9; Age: M=38, SD=3 months) were shown 16 20s video clips and 16 10s static images depicting two female adults interacting over a shared activity. Stimuli varied along 3 dimensions: (1) Gaze: mutual towards each other or towards the activity; (2) Distractors: many distractors or no distractors, where distractors were colorful toys; and (3) Motion: static image or video clip. Stimuli were counterbalanced across and within participants and eye tracking was used to evaluate patterns of attention. A 2nd order linear mixed model approach was used to examine attention to the scene, activities, people, and background elements.

Results: Decreased looking at the scene overall was associated with ASD ($p<.01$), fewer distractors ($p<.05$), and no motion ($p<.01$). TD participants looked more at the scene when motion was present (Group x motion interaction, $p<.01$). Decreased looking at activities was associated with ASD ($p<.01$), being in the younger age group ($p<.01$), the presence of more distractors ($p<.01$), and the lack of motion ($p<.01$). Older TD children looked more at activities than other groups (Group x age interaction, $p<.01$). Increased looking at the background was associated with ASD ($p<.01$), being younger ($p<.05$), more distractors ($p<.01$), and no motion ($p<.01$). Decreased looking at the people in the scene was associated with ASD ($p<.01$), being older ($p<.01$), more distractors ($p<.01$), and presence of motion ($p<.01$). Younger TD toddlers looked more at people than all other groups (Group x age interaction, $p<.01$). Eye tracking outcome measure associations with clinical characterization in ASD replicated previously observed findings.

Conclusions: Our results suggest that toddlers and children with ASD show a general pattern of diminished attention towards people and their activities. In typical development but not ASD, transitions consistent with a sharpening of attention towards the activities of others appear between 2 and 3 years of age. Interestingly, an effect of gaze direction was not present in the results of any outcome measures, suggesting that dynamic and complexity cues may play a greater role in shaping attention to scene-relevant context at these ages.

**106.017 17** Differences in Object Exploration Skills Between Infants at Risk for Autism and Typically Developing Infants in the First 15 Months of Life. I. Park*, M. Kaur, S. Srinivasan, A. N. Bhat and M. Sandbank, *University of Connecticut*

Background: Infants begin to grasp objects at six months of age and continue to explore various object properties based on shape, size, and texture. These fine motor skills lay the foundation for cognitive skills such as object knowledge as well as social communication skills such as hand gestures. Infants at risk for autism present with fine motor delays (Landa et al., 2005), which may affect their object exploration skills and therefore, indirectly influence their social communication and cognitive development.

Objectives: In the current study, we examined the differences in object exploration skills between infants at risk for autism (AU sibs) and typically developing (TD) infants and related them to infants' future social and motor outcomes.

Methods: 16 TD infants and 16 AU sibs were observed longitudinally at 6, 9, 12, and 15 months of age within an object exploration paradigm with developmental follow-up and autism screening conducted at 18 and 24 months. At each visit, infants were seated upright in a booster seat and were offered three different objects – a long rattle, a solid ball, and a circular, soft koosh ball. Videotaped data were coded for percent duration of oral, visual, and haptic exploration.

Results: At 6 months, TD infants demonstrated greater mouthing and grasping behaviors compared to AU sibs who showed greater visual fixation towards objects. At 9 months, TD infants began showing active control over objects with an increase in duration of grasping and purposeful object dropping behaviors; in contrast, AU sibs demonstrated a lower duration of grasping behavior and did not increase their dropping behavior until 12 and 15 months of age. At 15 months, the TD group continued to increase grasping behavior while the AU sibs group continued to show mouthing of objects. We will also report on differences between AU sibs who later developed developmental delays and ASD versus those who did not based on 18- and 24-month outcomes.

Conclusions: We believe that impairments in fine motor control and excessive object exploration

may contribute to the poor object exploration skills of AU sibs. Overall, our data suggest that object exploration may be an effective paradigm to assess fine motor and visual attention patterns of infants at risk for autism and could provide a window for early diagnosis of future autism-related motor and social impairments.

**106.018 18** Differences in Object Sharing and Locomotor Development Between Infants at Risk for Autism and Typically Developing Infants in the First 15 Months of Life. S. Srinivasan*, M. Kaur and A. N. Bhat, *University of Connecticut*

Background: Older infants engage in triadic joint attention to share object play with their caregivers (Bakeman & Adamson, 1984). Infants move in different ways to express their intent to share by turning to look, pointing to, showing objects, giving objects, vocalizing, or approaching the caregivers with objects. Advancements in locomotor skills could facilitate a child's object sharing or joint attention bids (Karasik et al., 2011). Young children who later develop Autism Spectrum Disorders (ASDs) show social as well as motor impairments. Moreover, early motor impairments may facilitate social impairments in young infants at risk for ASDs (i.e. infant siblings of children with ASDs or AU sibs).

Objectives: In the present study, we compared object sharing behaviors between AU sibs and typically developing (TD) infants at 9, 12, and 15 months. In addition, we examined the influence of locomotor development on the object sharing abilities of both groups of infants.

Methods: 16 AU sibs and 16 TD infants were observed during an object sharing task at 9, 12, and 15 months with developmental follow-up and autism screening at 18 and 24 months. During each visit we collected video data for 14 minutes wherein infants were seated facing their caregivers near multiple small toys. In the spontaneous condition (7 minutes), the caregiver was asked to be quiet and wait for the child to initiate a social interaction. In the social condition (7 minutes), the caregiver initiated a clean up activity wherein they pointed to the toy and asked the child for a particular toy. Dependent variables included total rates and types of object sharing bids including throws, reaches, approaches towards CG without objects, and approaches with objects. In addition, we grouped infants by locomotor status at each visit (i.e.; crawlers or walkers).

Results: Rates of object sharing bids were greater in the social condition than the spontaneous condition. In addition, object sharing interacted with motor skill level in both groups of infants. Specifically, infants with advanced locomotor skills i.e.; walkers showed greater rates and variety of object sharing behaviors than crawlers. AU sibs had lower rates of object sharing bids, specifically in the social condition compared to TD infants. Differences between TD infants and AU sibs were significant among walkers but not in crawlers. Moreover, AU sibs with poor social communication and motor delays had lower rates of sharing than AU sibs without social communication and motor delays.

Conclusions: Our results suggest that object sharing behaviors may provide an early marker for future risk of ASDs within the first year of life. Moreover, early fine motor and gross motor delays may contribute to the social communication delays in infants at risk for ASDs. Therefore, it would be important to facilitate these social actions as well as motor development during treatment sessions of infants at risk for ASDs.

**106.019 19** Differences in Overt but Not Covert Gaze-Following in Young Infants at Risk for Autism Spectrum Disorders. K. A. Rice*, E. Wood, R. S. Newman, N. B. Ratner, J. Lidz and E. Redcay, *University of Maryland*

Background: Children and adults with autism spectrum disorders (ASD) show abnormalities in real-world gaze monitoring, but often perform typically in laboratory-based paradigms examining gaze cueing. Two types of gaze cueing—both present from infancy in typical development—often appear intact in ASD: overt (i.e., looking in the direction of gaze) and covert (i.e., faster detection of gaze-cued targets). Typical cueing responses in children with ASD could either suggest that gaze cueing is typical in autism or that performance is achieved via learned alternative mechanisms. Examining gaze cueing in infants at risk for ASD could disambiguate these possibilities and may reveal an early marker of autism.

Objectives: This study used a Posner-style gaze cueing paradigm to examine how infants at low risk (LR) and high risk (HR) for ASD overtly and covertly respond to gaze, and investigated how this responsivity predicted future social and cognitive functioning.

Methods: Thirty-seven infants (9 HR) aged three to five months viewed trials in which a face appeared on-screen and shifted gaze to the left or right. One second after this shift, the face disappeared and a target appeared either on the side congruent, or incongruent, with the gaze. Infant eye movements were videotaped and coded by blinded researchers. Covert response to gaze was measured using the latency of the infant's look to the target. Overt responses were defined as looks in the direction of the on-screen gaze shift at least 100ms after the shift, but before the target appeared.

Results: There was no difference between groups in the time to congruent versus incongruent targets (e.g., covert gaze cueing), although for neither group was the effect significant. The LR group, however, was significantly more likely to overtly follow gaze before the target appeared ($p<.001$). There was no group difference in error rates for overt cueing (e.g., shifting left after rightward gaze). For LR infants, errors in overt responding predicted worse communicative ($r=-.64$, $p<.05$) and social ($r=-.69$, $p<.01$) skills at 12 months on the Ages and Stages Questionnaire. These correlations were in the opposite (positive) direction, although not significant, for the HR group.

Conclusions: Past research has suggested that gaze cueing can rely on physical (e.g., pupil movement) or social (e.g., understanding intention) routes, and that physical factors may explain intact gaze cueing in ASD. Consistent with these findings, covert gaze cueing is not impaired in HR infants. At-risk infants, however, do show an atypical overt gaze-following response; compared to LR infants, HR infants are less likely to correctly follow gaze shifts before a target appears. This suggests a potential dissociation between the mechanisms of overt and covert cueing, and future studies should explicitly test this possibility. Further, though the small sample precludes definitive conclusions, the processes underlying gaze behavior may differ between LR and HR infants, as a behavior that predicts worse social outcomes for LR infants (looking indiscriminately away from the face) does not appear to serve the same function in HR infants. Future research will examine how these responses relate to diagnostic outcomes.

**106.020 20** Different Sources of Parenting Stress in Families of Toddlers with ASD or DD. L. D. Haisley*, M. L. Barton and D. A. Fein, *University of Connecticut*

Background:

Parents of children with an autism spectrum disorder (ASD) have consistently been found to experience higher levels of parenting stress, than parents of children with other disabilities. Studies have linked this heightened stress to ASD specific characteristics (social skills, communication, repetitive behaviors), as well as more general child characteristics (behavior problems, daily living skills). Importantly, studies are beginning to address how parent/family factors contribute to parenting stress. However, most of these studies have looked at parenting stress in families with children in middle childhood and beyond, and few have addressed the issue of social support.

Objectives:

This study extends previous research on the experience of parenting stress in families of young children with an ASD. Specifically what child, parent and family factors contribute to the experience of stress at the time the child is diagnosed, and how do these differ from the factors that contribute to stress in families of children with a Developmental Delay (DD).

Methods:

Data were drawn from a study assessing the validity of the M-CHAT/-R screening tools. Parenting stress was measured using the Parenting Stress- Short Form (PSI-SF) with parents of 89 children with an ASD (mean age=25.1 months) and 48 children with a DD (mean age=24.8 months). Parents were also given a caregiver information questionnaire, the Vineland- II and the Social Support Index. Children were assessed using the ADOS, CARS, and Mullen Scales of Early Learning.

Results:

Contrary to previous studies, total level of parenting stress did not differ in the parents of children with an ASD ($M=77.18$, $SD=21.19$) or a DD ($M=81.19$, $SD=23.50$), $t(135)=1.04$, $p=034$. CARS Total was associated with higher stress in the ASD group ($r=.22$, $p=.04$), but not the DD group. Additionally higher scores on both

expressive and receptive language domains on the Mullen were associated with higher levels of stress in the ASD but not the DD group, (r=.25, p=.02; r=.27, p=.01). Finally, lower scores on the Vineland-II Social domain were related to higher levels of total stress in the ASD, but not the DD group (r=-.24, p=.03). Higher levels of social support showed a moderate association with lower parenting stress in both ASD and DD groups. Overall social support did not significantly moderate the effect of symptom severity on parenting stress in the ASD group; more specific moderators will be explored.

Conclusions:

Parents of two-year-old children with an ASD or DD were shown to experience similar levels of parenting stress. While stress in the ASD group was associated with ASD specific behaviors and higher language skills, the same was not true for the DD group. The finding that higher language skills are associated with parenting stress might suggest that as children become more verbal, their ASD-specific symptoms might become more apparent, causing the parent distress. Additional hypotheses on the experience of stress in the DD group will be examined. The differences between ASD and DD groups suggest early differences in the experience of parenting children with an ASD and those with DD; however both lead to experiences of distress.

**106.021 21** Early Developmental Trajectories of Social Communication in Infants at Risk for ASD. L. A. Edwards*[1], K. E. Masyn[2], R. Luyster[3] and C. A. Nelson[4], (1)*Harvard University, Boston Children's Hospital*, (2)*Harvard University*, (3)*Emerson College*, (4)*Boston Children's Hospital*

Background: Siblings of children with autism spectrum disorders (ASD) are at increased risk for developing an ASD. By prospectively studying the younger siblings of children with an ASD (high risk for ASD, or HRA), as well as children without an ASD (low risk controls, or LRC), we may identify endophenotypes of ASD risk and predictors of ASD outcomes; such advances could enable earlier intervention and diagnosis – and improved outcomes – for affected individuals. In this study we seek to identify endophenotypes and diagnostic predictors of autism, by modeling the longitudinal trajectories of early social communication behaviors in HRA and LRC infants.

Objectives: In this study, we investigate the trajectories along which social communication behaviors develop in a sample of HRA and LRC infants; we examine the extent to which ASD risk predicts the trajectories of these behaviors; and we determine whether and which early social communication trajectories predict later ASD diagnoses.

Methods: Parents of 127 HRA and 119 LRC infants filled out the Communication and Symbolic Behavior Scales (CSBS) and the MacArthur-Bates Communicative Development Inventory (MCDI) when their children were 6, 9, 12 and 18 months old. Raw scores from CSBS social and symbolic subscales and MCDI gestures were modeled as a social communication factor using confirmatory factor analysis. Growth mixture modeling was then used to divide individuals into latent classes based on their social communication trajectories. Risk status was related to class membership, and the proportion of ASD diagnoses within each class was estimated for the subset of children who had confirmed diagnostic outcomes (N(typically developing) = 122; N(ASD) = 21; N(non-ASD disorder) = 3).

Results: A 3-class solution was optimal. Class 1 comprised children with high social communication scores and accelerated social communication development between 6 and 12 months (28.0% of the sample); Class 2 comprised children with intermediate social communication scores and a roughly linear developmental trajectory from 6 to 18 months (58.3% of the sample). Class 3 comprised children with low social communication scores, and decelerated social communication development between 6 and 12 months (13.8% of the sample). HRA infants were significantly more likely than LRC to be in class 3 than either class 1 (odds-ratio = 7.19, $p$ <0.01) or 2 (odds-ratio = 5.17, $p$ = 0.02). Class membership was not predicted by the infants' sex. ASD diagnoses were significantly predicted by class membership ($\chi^2(2) = 7.46$, $p = 0.02$) such that only 6% of the individuals with outcomes in Class 1, but 12% of those in Class 2 and 38% of those in class 3 developed ASD.

Conclusions: On parent-reported measures, infants at high risk for ASD were more likely to have lower social communication abilities and decelerated early social development compared to children without an ASD sibling. Infants belonging

to the class exhibiting the lowest scores and slowest early development of social communication abilities were also significantly more likely to develop ASD. Given the relatively small sample examined herein, these results will be confirmed and extended using Bayesian estimation.

**106.022 22** Early Intervention for Autism and Parental Stress As an Outcome Measure: Insights from Treatment As Usual. A. Narzisi*[1], C. Colombi[2], S. Calderoni[3], G. Balboni[4] and F. Muratori[5], (1)*University of Pisa - Stella Maris Scientific Institute*, (2)*University of Michigan*, (3)*Magnetic Resonance Laboratory, Division of Child Neurology and Psychiatry University of Pisa; Stella Maris Scientific Institute*, (4)*University of Pisa*, (5)*Stella Maris Scientific Institute*

**Background:**

Few studies have deeply examined the question of whether parents' stress levels affect their children's progress in intervention. If by one side the research underlines the negative impact of the parent stress on outcome of children, another bulk of evidence pleads in favour of a different trend in parental stress with high parental stress at baseline evaluation linked to a better treatment outcome.

**Objectives:**

The aim was to examine the parental stress, as an outcome measure, after 6 months of treatment as usual (TAU).

**Methods:**

The sample consisted of 68 children (mean age: 2,94; sd: 0,79). At T0, 48 received a DSM-IV-TR diagnosis of Autism and 20 of PDD-NOS. At T0, 56 received an ADOS-G diagnostic classification of Autism and 12 of Spectrum. The ADOS-Calibrated Severity Score (CSS) of 68 children was 7,4 (± 0,83). The Griffiths Performance Development Quotient was of 73,5 (sd: 14,54). All children were at their first diagnosis of ASD and all parents filled out Parenting Stress Index (PSI) for two times (T0 and T1).

**Results:**

After 6 months of TAU, PSI mean scores showed a significant betterment. At T1, CSS improved in 37 of 68 children (Positive Outcome) while it was the same or worsed in 31 of 68 (No Positive Outcome).

At T0, PO and NPO groups did not differ significantly from each other on age ($P$ = .432) and CSS ($P$ = .073).

Regarding PSI at T0, analyses revealed significant higher mean scores for the PO group than the NPO on the scales Parent Domain (P= .046), Depression (P=.038), Health (P=.005) and Life Stress (P=.004).

At T1, no significant differences between PO versus NPO in terms of weekly hours of TAUs were found ($P$ = .654). However, a significant difference between groups on time of TAUs 'with the direct involving of parents' was found (P = .048). No significant differences, between PO and NPO, were showed at T1 in all PSI scales.

The PSI Total scores obtained at T0 were correlated with the CSS change (T1-T0) separately in both the PO and NPO groups. The CSS change (Δ T1-T0) correlated at a highly significant level in the PO group (r = -,389; P = .017). In other words, the more stressed the family the greater was the improvement in CSS. In contrast, there was a non-significant negative correlation of PSI Total with CSS change in the NPO (r = -,275; P = .134).

**Conclusions:**

Results showed a global improvement in parental stress after an early TAU. The study showed that PO are characterized by higher parental stress levels at T0 than NPO. However, PO showed significant lower parental stress levels at T1 than NPO. In the PO, the higher parental stress levels could be given by their awareness about the presence of a developmental problem in own children and probably this awareness could help the parents in the search of a better treatment solution (for example parents of PO were significantly involved in the treatment than parents of NPO).

**106.023 23** Electrophysiological Indices of Biological Motion and Audio-Visual Integration in Infants at Risk for Autism. H. S. Reuman*[1], R. Tillman[1], E. Levy[1], G. Righi[1], M. Rolison[1], C. E. Mukerji[1], A. Naples[1], M. Coffman[2], P. Hashim[3] and J. McPartland[1], (1)*Yale University*, (2)*Virginia Polytechnic Institute and State University*, (3)*Yale University School of Medicine*

Background: Perceptual sensitivity to biological motion (BM) is evident in infants as young as two days old and is hypothesized to underpin development of more sophisticated social behaviors. Similarly, audio-visual (AV) integration, or the detection of a temporal contingency between auditory and visual events, is also evident in infancy and is a critical developmental ability. Behavioral studies suggest that toddlers with autism spectrum disorder (ASD) demonstrate atypical BM perception and display preferential attention to AVS (audio-visual synchrony) in comparison to unimodal stimuli. These early processing atypicalities may represent early predictors of autism.

Objectives: This study applied event-related potentials (ERPs) to contrast neural responses to BM and AV integration in infants at high-risk (HR) and normal-risk (NR) for ASD. By investigating electrophysiological markers of BM and AV events, we aimed to (a) assess potential hyposensitivity to BM in HR infants, (b) identify intact/enhanced integration of AV events in HR relative to NR infants, and (c) compare developmental trajectories of typical and atypical neural responses to BM and AVS prior to the emergence of behavioral symptoms in ASD.

Methods: HR (n= 25) and NR (n= 40) infants were assessed at three-month intervals between 3 and 12 months of age. EEG was recorded with a 128-channel Hydrocel Geodesic Sensor net while infants viewed point-light displays depicting BM and scrambled motion (SM; Experiment 1) or unimodal/bimodal auditory (tone) and visual (circle) stimuli (Experiment 2). In Experiment 1, ERPs evoked by BM or SM (N200, a negative deflection over right occipitotemporal scalp between 200-300 ms; PSW, a late anterior positive slow wave between 900-1500 ms) and event-related oscillations (EROs) in the mu range (6-9 Hz), indicating activity of the action perception system, were computed. In Experiment 2, ERPs evoked by audio, visual, and AV presentations (N100, a negative deflection over fronto-central scalp between 80-130 ms) and EROs in the gamma range (20-100 Hz), indicating activity of integration mechanisms, were computed.

Results: In Experiment 1, neither NR nor HR differentiated between BM and SM at the N200 at 6 months (*p*s>.05). At 12 months, only NR infants displayed emergent differentiation of the N200 elicited by BM and SM ($p$=.019). At 6 months, NR infants exhibited enhanced amplitude of the PSW to BM relative to HR infants ($p$<.05). Between 9-12 months, HR infants failed to display expected attenuation of EEG mu rhythm to BM ($p$=0.65) relative to NR infants ($p$=.038). In Experiment 2, NR but not HR infants displayed expected sensitivity to AV integration at the N100; the N100 AV response in NR infants was more negative than the summed response of audio-only and visual-only.

Conclusions: Infants at risk for autism demonstrated atypical neural responses at electrophysiological markers of both social and basic sensory perception. These findings suggest that, rather than focal anomalies in social perceptual brain circuitry, distributed perceptual differences, including those affecting multisensory integration, may underlie autistic symptomatology. The study demonstrates that use of complementary measures of brain function may shed light on factors associated with risk status and eventual diagnosis of ASD.

**106.024 24** Goal Anticipation in Toddlers with ASD and High-Risk Siblings of Children with ASD. S. Thomas*[1], J. Parish-Morris[2], K. Spielman[1], E. N. Cannon[3], A. L. Woodward[4], J. Pandey[1], R. T. Schultz[1] and S. Paterson[1], (1)*The Children's Hospital of Philadelphia*, (2)*University of Pennsylvania and Children's Hospital of Philadelphia*, (3)*University of Maryland, College Park*, (4)*University of Chicago*

**Background:** Typically developing infants interpret actions by assigning intentions and goals to human characters, but not to inanimate objects, such as grasping claws (Cannon & Woodward, 2011). Although some research suggests that children with ASD are able to recognize goals and intentions (Carpenter et al., 2001; Hamilton, 2009), other findings suggest that their ability to use social information about intentionality in the service of other goals such as motor imitation or word learning is impaired (Parish-Morris et al., 2007; Somogyi et al., 2013). With few exceptions, studies of intentionality in ASD focus primarily on middle childhood; little research has explored the development of goals and intentions in toddlers.

**Objectives:** Using an established paradigm developed by Cannon and Woodward (2011), we aim to determine whether toddlers with Autism Spectrum Disorder (ASD) and those at high-risk

for ASD attribute goals to a reaching action performed by a human arm vs. a mechanical claw.

**Methods:** Toddlers with autism (N=8) and siblings of a child with autism (N=21; Mean age=30.80 months, range: 23.9-39.6) were randomly assigned to watch a short video of a reaching action performed by either a hand (N=16) or a mechanical claw (N=13). Gaze data was recorded using a Tobii infrared eye tracker. Four identical blocks included 3 familiarization trials (hand or claw reaches toward one of two toys) and 1 test trial each. In test trials, the toys switched places, and the video showed the hand or claw beginning to reach, but stopping short of choosing an object. An experimenter blind to diagnostic status coded children's anticipatory looks during the test trials.

**Results:** A multivariate GLM controlling for nonverbal mental age revealed that, in contrast to prior research with typical infants, toddlers across both groups looked equally at the goal object and the location of the familiarized reach during test trials in both conditions, $F(2,25)=2.28$, $p=0.14$. This suggests that children with ASD and high-risk siblings do not demonstrate differential goal attribution to human actors vs. mechanical claws, which is consistent with prior studies showing reduced attention to social information and less automated interpretation of actions as goal-oriented. Thus, this finding could relate to symptoms of ASD and features of the broader autism phenotype. An alternative explanation is that older children simply do not make anticipatory looks to goal objects in this paradigm; data on matched typical toddlers is currently being collected to tease apart these two possibilities.

**Conclusions:** These results have implications for how we understand the development of social cognition and social skill in ASD and siblings at risk, as understanding goals and intentions is a building block for later theory of mind. Current data collection with a typically developing control group of the same age and developmental level will shed further light on our findings.

**106.025 25** High-Risk Siblings with Atypical Developmental Trajectories: Clinical Outcomes at Early School Age. K. D. Tsatsanis*[1], K. K. Powell[1] and K. Chawarska[2], (1)*Child Study Center, Yale University School of Medicine*, (2)*Yale University School of Medicine*

Background: Prospective studies of siblings of children with ASD (high risk (HR)) indicate highly variable and vulnerable developmental trajectories in the first 3 years of life but little is known beyond this age.

Objectives: To examine clinical outcomes in a group of complex cases ascertained though the prospective longitudinal HR sibling study from 6 to 36 months.

Methods: Six HR siblings with complex clinical presentations in the first 3 years of life (i.e., borderline and fluctuating ASD symptoms) were comprehensively assessed at the age of 4-6 years, using a battery comprised of cognitive, neuropsychological, language, adaptive, social and emotional functioning measures.

Results: *Clinician Best Estimate.* Four of the six children continued to evidence social pragmatic difficulties at follow-up, but were subthreshold for ASD. One child met criteria for ADHD and Anxiety-NOS. Of the two children who previously received a PDD-NOS diagnosis, one met criteria for ASD and the other showed no evidence of ASD. *ASD Symptom Severity.* In all but one case, ASD symptom severity declined or remained stable between 3 and 6 years. Level of ASD related symptoms on the ADOS ranged from 'minimal' to 'low'. Infrequently observed were unusual sensory interests, or restricted, repetitive patterns of behavior or interests. *Comorbid symptoms.* The Early Childhood Inventory-4 revealed clinical or borderline range scores for Generalized Anxiety Disorder, Social Phobia, or ADHD. Two children had elevated global scores on the BRIEF suggesting the presence of executive functioning vulnerabilities. No children had a significant elevation on the Shift scale (assessing flexibility/adaptability), a scale that typically distinguishes children with ASD from other clinical groups. *Cognitive functioning.* All children were functioning in the average to above average range; in two cases verbal IQ scores exceeded nonverbal IQ scores by at least 1 standard deviation (SD). *Language.* All children's core language fell in the average to above average range. In four out of six cases, narrative skills fell at least 1SD below their formal language production. *Adaptive Functioning.* All but one child had a Socialization score in the 'Adequate' range on the Vineland-II. However, examining interpersonal skills, three of the six were

functioning below age-based expectations. *Social Perception*: Scores on measures of affect recognition, memory for faces, and memory for names were lower than cognitive ability by at least 1SD in 50-75% of children.

Conclusions: These preliminary data underscore the complexity of long-term outcomes in HR siblings. A common theme suggests that variability is a defining feature of their presentation as these children evidenced variable developmental trajectories and variable diagnostic outcomes; a co-occurring vulnerability for both ASD symptomatology and other disorders exists on a clinical and also on a subclinical level. This variability highlights the danger of an "averaging artifact" where the pattern detected at a group level does not describe well any single member of the group. Understanding the full range of outcomes among HR siblings in future research, in terms of categorical presentation and functioning along specific dimensions, will be crucial for understanding the risk factors and clinical needs of this unique population.

**106.026 26** Identifying Unique and Shared Pre- and Perinatal Risk Factors in Simplex Versus Multiplex ASD and ADHD Families. A. Sluiter-Oerlemans*[1], M. J. Burmanje[2], C. A. Hartman[3], B. Franke[4], J. K. Buitelaar[4] and N. N. J. Rommelse[1], (1)*Donders Institute for Brain, Cognition and Behavior, Radboud university medical center*, (2)*Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Centre*, (3)*University of Groningen and University Medical Center Groningen*, (4)*Radboud university medical center*

**Background:** Autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD) are highly heritable, heterogeneous neurodevelopmental disorders that co-occur frequently. Some studies show that the high co-morbidity is caused by shared genetic factors, but it is also possible that the high co-morbidity rates of ASD and ADHD are caused by shared pre- and perinatal risk factors. A more complete understanding of the complex etiologies of ASD and ADHD may be helpful in improving treatment and prevention.

**Objectives:** The current study aims to a) identify pre- and perinatal risk factors associated with ASD, ADHD, or both disorders and b) examine whether these factors are unique, i.e., only found in affected offspring, or shared, i.e. also present in non-affected offspring, by stratifying into simplex (SPX; one affected individual within a family) and multiplex (MPX; two or more affected individuals) families, respectively. So far, studies have suggested that in ASD, pre- and perinatal risk factors are more unique to the affected child (likely to be found in SPX families), whereas in ADHD, risk factors were more often shared between affected and unaffected siblings (likely to be found in MPX families).

**Methods:** Pre- and perinatal data were collected in 56 ASD and 31 ADHD SPX families (including: 56/31 probands and 81/55 unaffected siblings, respectively) and 59 ASD and 171 ADHD MPX families (including 96/270 probands and 55/128 unaffected siblings, respectively) and 203 control families (408 children), using retrospective parent-report questionnaires. Thirteen pre- and perinatal risk factors were examined, including miscarriages/bleeding, maternal diseases, infections or intoxications during pregnancy, stress during pregnancy, labor/parturition, prematurity (<37 weeks), suboptimal condition of the child at birth, being firstborn, artificial pregnancy, maternal and paternal age at conception, and birth weight.

**Results:** No pre- and perinatal risk factors were related to both disorders. The risk factors stress during pregnancy, suboptimal condition of child at birth, maternal infections and labor/parturition were identified for ASD. The first two factors emerged only in SPX probands, whilst the latter two risk factors were observed only in MPX probands. In ADHD families, the risk factors low parental age (present in both SPX and MPX families) and maternal diseases during pregnancy (MPX families only) were identified. These factors were shared between affected and unaffected siblings.

**Conclusions:** Our results suggest that the high co-morbidity of ASD and ADHD cannot be explained by shared pre- and perinatal risk factors. Instead, these factors might have a formative influence on which disorder (ASD or ADHD) a person will develop. Particularly in ASD, pre-and perinatal risk factors differed between the SPX-MPX families. As expected, risk factors in ASD families were not shared between affected and unaffected siblings, which indicated that these factors may have a unique, possible determining effect on the development of the disorder. In ADHD, risk factors were shared

between siblings, suggesting that these factors might increase familial risk for ADHD.

**106.027 27** Interest in Potential Reinforcers in the Second Year of Life Predicts Outcome of Behavioral Intervention in Toddlers with ASD. L. Klintwall*[1], S. Macari[2], S. Eikeseth[1] and K. Chawarska[2], (1)*Oslo & Akershus University College*, (2)*Yale University School of Medicine*

Background: There is substantial variation in language and intellectual outcomes in children with ASD. A recent study suggests that the number of stimuli that children find reinforcing may constitute a predictor of response to behavioral treatment in preschool-aged children with ASD (Klintwall & Eikeseth, 2012). However, very little is known if a similar effect can be found in children presenting for a differential diagnosis of ASD in the second year of life. Advancing our understanding of factors that affect amenability to treatment at the very early stages of ASD emergence would improve our ability to individualize treatments very early on and to enhance outcome in the affected children. Moreover, in contrast with our original work, which was based on informant report, in this study we intended to design and test a coding system based on children's responses to play probes in the context of semi-structured interaction with an examiner.

Objectives: To address this gap we investigated child interest in objects and activities during the Autism Diagnostic Observation Schedule-Toddler Module (ADOS-T; Lord et al, 2000) assessment as a predictor of subsequent development measured by adaptive behavior and verbal and non-verbal developmental quotient (DQ) at ages 2-4 years.

Methods: Reinforcing function of stimuli can be approximated from exhibited affect and attention towards the object or activity. Based on our previous work (Klintwall & Eikeseth, 2012), we developed a novel scoring system for capturing toddlers' interest in potential reinforcers (e.g. edibles, toys): the Assessment of Volition and Object Curiosity (AVOC). The scoring system yields a mean interest score. AVOC was used to score video recordings of 70 toddlers with ASD who underwent assessment between 14 and 32 months (Time 1). Developmental (Mullen Scales of Early Learning; Mullen, 1995) and adaptive skills (Vineland Adaptive Behaviors Scales-II; Sparrow, et al., 2005) were measured concurrently and then again when the children were 21 to 49 months old (Time 2). Between measurements, the children received a variety of community-based behavioral and developmental interventions**.**

Results: The AVOC scoring system exhibited acceptable levels of test-retest (0.80) and inter-rater reliability (0.90). AVOC score, ADOS-T total score, Mullen verbal and nonverbal DQ, and Vineland adaptive full scale score (Adaptive Behavior Composite; VABC) was entered into linear regression models at Time 1 to predict outcome at Time 2 defined as VABC, verbal DQ and non-verbal DQ**.** The AVOC score was the only significant predictor of Time 2 adaptive behavior ($p=.001$, $R^2=.394$) as well as non-verbal DQ ($p=.024$, $R^2=.277$), outperforming Time 1 verbal DQ ($p=.216$ and $p=.226$, respectively), non-verbal DQ ($p=.652$ and $p=.856$) and ADOS-T scores ($p=.305$ and $p=.285$). AVOC score at Time 1 also contributed, along with non-verbal DQ, to variance in verbal DQ at Time 2 ($p=.009$, $R^2=.318$).

Conclusions:

Interest in potential reinforcers was a powerful predictor of subsequent development for toddlers with ASD. Future studies should aim to evaluate and develop techniques for identifying and expanding the repertoire of stimuli functioning as reinforcers for children who score low on the AVOC, thus possibly improving their outcomes.

**106.028 28** Limited Influence By Others' Gaze Direction on Initial Object Processing in Three-Year-Olds with Autism. T. Falck-Ytter[1], E. Thorup*[2] and S. Bolte[1], (1)*Karolinska Institutet*, (2)*Uppsala Child & Babylab*

Background:

The ability to follow other peoples' gaze is a key component of joint attention, and plays an important part in early development of areas such as social interaction and language. An early deficit in joint attention behavior is clinically considered a prominent feature of Autism Spectrum Disorders (ASDs). To identify the exact nature of this deficit has however proved difficult. Experimental studies assessing spontaneous gaze following have yielded mixed results, with some finding autistic children to display lower gaze following accuracy and others not. A recent study found that infants with later emerging socio-communicative problems, although accurate in gaze following,

spent less time looking at the (by another person) attended object than did other children. This was interpreted as reflecting a failure to understand the communicative meaning of the other's joint attention bid.

Objectives:

The aim of the present eye tracking study was to investigate gaze following in preschoolers with ASD using duration of the first fixation to the attended and unattended objects respectively as the primary measure. First fixation duration has been suggested to work as a measure of visual information acquisition, and since real life interactions are usually fast, we believe it to be a more ecologically valid measure than comparisons of total looking time.

Methods:

The study included a group of three-year olds with ASD (n=12), a control group of age matched typically developing (TD) children (n=14), as well as a group of children with other developmental delays (DD, n=9). The stimuli were videos of a female model turning to look at one out of two present objects. The subsequent analysis included measures of accuracy (i.e. the tendency to look at the same object as the model) as well as first fixation durations to the attended vs. unattended objects.

Results:

The analysis revealed no group differences in terms of accuracy, and all groups made more congruent gaze shifts than expected by change (ASD $p$ = 0.003; DD $p$ = 0.011; TD $p$ = 0.005). In terms of first fixation duration, the three groups performed differently ($p$ = 0.007). The TD and the DD groups produced longer first fixations at the attended object than did the ASD group ($p$ = 0.04 and $p$ = 0.002 respectively; first fixation duration at unattended object used as baseline).

Conclusions:

We found that, although accurate in gaze following, the children in the ASD group did not differentiate between the two objects in terms of first fixation duration. This suggests that initial object processing is less influenced by other people's gaze direction in ASD. Lack of immediate allocation of processing resources to the objects others attend to may have negative impact on learning opportunities during social interaction.

**106.029 29** Longitudinal Retrospective Video Analysis of Object Play in Infants with Autism. K. P. Wilson*[1], H. Wiener[2], M. DeRamus[3], J. Bulluck[3], G. T. Baranek[3], L. R. Watson[3] and E. R. Crais[3], (1)*Kennedy Krieger Institute*, (2)*Hilltop Home*, (3)*University of North Carolina at Chapel Hill*

Background: Existing research describes the atypical nature of play behaviors in young children (toddler age and older) with autism; however, little is reported about the earliest play behaviors of infants who are later diagnosed with autism. This study examined the play behaviors of three groups of infants (typically developing, later diagnosed with autism, and later diagnosed with developmental delay) in order to elucidate early patterns of play behavior and inform decisions regarding early diagnosis and intervention.
Objectives: This presentation will focus on the following three objectives: (1) to describe play behaviors in the three groups of infants; (2) to examine group differences in play, including highest level of play achieved; and (3) to examine correlations between highest level of play achieved during infancy and later developmental outcomes (i.e., Vineland Adaptive Behavior Scale, Childhood Autism Rating Scale, IQ).
Methods: This study compared object play of three groups of infants (total n=92) at two time points (9-12 months and 15-18 months) using longitudinal retrospective video analysis of infants as seen in naturalistic home video contexts (e.g., birthday parties, outdoor play). Videos were matched by content factors and an established electronic coding system was used. Analyses included both descriptive and inferential methods. A unique combination of regression models (i.e., tobit and logistic) was used to examine differences between groups, and non-parametric correlations were utilized to determine relationships between early play and later outcomes.
Results: Descriptive analyses indicated that, across groups, the majority of time was spent in exploratory play, and that the highest levels of play (i.e., functional+symbolic) were exhibited by 41% of typically developing infants, but only by 13% with developmental disabilities and 9% with autism. Results of the regression analyses similarly showed that infants later diagnosed with autism used significantly less high level play than did typically-developing infants (p=.034, OR=11.47). Finally, significant correlations were

found between the highest level of play achieved by the atypically developing infants (those later diagnosed with a developmental disability or autism) at 15-18 months and their preschool VABS (r=.255, p=.029) and IQ (r=.236, p=.042) scores.
Conclusions: Combined results not only support the importance of play in early diagnosis and intervention of developmental disabilities including autism, but also elucidate key differences in play at these early stages of development. Interestingly, the logistic analysis results suggest that the presence or absence (vs. duration, variety, flexibility) of high levels of play in the first two years of life as a potentially useful tool for diagnosticians, early interventionists and caregivers. This study not only adds to the literature through the observation of naturalistic video footage, which may be more representative of everyday play patterns, but also through the careful coding and analysis of data using methodology best suited to the unique nature of this type of data set.

**106.030 30** Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) Validation in Portugal - Preliminary Findings. C. C. Almeida*[1], A. Rodrigues[2] and D. Robins[3], (1)*PIN*, (2)*Faculdade Motricidade Humana*, (3)*Georgia State University*

Background:

Autism Spectrum Disorder (ASD) screening has been recommended as a way to start early intervention as soon as possible in order to improve outcomes. However, screening is not yet a common procedure in Portugal. In order to promote ASD screening, using a tool validated in other countries, an M-CHAT-R study has been started with the collaboration of Georgia State University. Preliminary findings are presented.

Objectives:

The main goal of this study is to start the validation of the Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) in Portugal as a screening tool for low-risk toddlers.

Methods:

Toddlers are recruited from two sources: childcare centers and pediatric check-ups. To date, 485 toddlers between 16 and 30 months (*m*=23.01, SD=3.92) were screened with M-CHAT-R. Parents of toddlers at risk on M-CHAT-R completed the M-CHAT-R Follow-up as an interview, and those who continued to show risk were evaluated using Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview Revised (ADI-R) and Griffiths Mental Development Scale.

Results:

From the 391 screened in daycare, 34 were positive (8.7%). After the Follow-up, six continued to screen positive and three were diagnosed with an ASD, two were typically developing and one had a developmental delay. From the 94 toddlers screened in pediatricians settings, eight were positive (8.5%), after the Follow-up two continued to screen positive; neither one was diagnosed with ASD (one had a developmental delay).

Conclusions:

Across the two groups, the M-CHAT-R performed similarly (8.7 vs 8.5% screened positive initially), suggesting that it is important to screen in multiple settings until screening is thoroughly incorporated into well-child care. The M-CHAT-R appears to be performing similarly to other countries' studies, such as in the US and Spain. Professionals from daycares seem more willing to screen than pediatricians during check-ups. Portugal requires more information and awareness about ASD screening to help children at risk for ASD get identified and into early intervention as young as possible.

**106.031 31** Predicting Toddlers' and Preschoolers' Attentional Skills and Sensory Features from Attentional Profiles on the First Year Inventory. M. G. Sabatos-DeVito*[1], R. Stephens[2], J. S. Reznick[2], L. R. Watson[3], G. T. Baranek[2] and J. Chen[4], (1)*UNC-Chapel Hill*, (2)*University of North Carolina at Chapel Hill*, (3)*University of North Carolina*, (4)*University of North Carolina-Chapel Hill*

Background: The First Year Inventory (FYI; Reznick et al., 2007) is a parent questionnaire designed to detect 12-month-old infants at risk for a diagnosis of Autism Spectrum Disorders (ASDs). The current scoring metric, based on cut-off scores in social-communication and sensory-regulatory domains, is effective in detecting some infants who receive an ASD diagnosis, and others with developmental concerns; however, not all children who develop ASD could be detected with the FYI (Turner-Brown et al., 2012). Attentional differences and sensory response patterns are

evident early in development for those diagnosed with ASDs. Exploring new dimensional constructs for the FYI may improve our understanding of different profiles that predict attentional and sensory differences, and risk for ASD and other developmental disorders, and can inform interventions.

Objectives: The purpose of this study was to establish constructs of attention relevant to the development of ASDs using the FYI items, validate those constructs with clinical measures of attention and sensory features, and investigate their predictive value.

Methods: We developed three new constructs from the original FYI items to tap dimensions of attention: (a) overfocused attention (OFA), (b) initiating joint attention (IJA), and (c) responding joint attention (RJA). Constructs were identified through literature reviews, theoretical considerations, and statistical analyses of an extant database with 7,823 FYIs. These constructs were further validated by analyzing assessments of attention and sensory features of 63 children (Mean Age = 14.14, SD = .78) who scored at risk on the FYI and were evaluated as part of a larger study. Correlational analyses of the new constructs were conducted with the Early Childhood Behavior Questionnaire (ECBQ; Putnam et al., 2006) and Sensory Experiences Questionnaire (SEQ; Baranek et al., 2006). Attention and sensory measures are being collected at ages 2 and 3 to demonstrate predictive validity of the new constructs, and explore relations with sensory features.

Results: The new constructs demonstrate good Cronbach alpha coefficients: IJA (*Alpha*=0.763), RJA (*Alpha*=0.723), and OFA (*Alpha*=0.699). Positive, significant correlations ($p<.0001$) with the original FYI subdomains were found: IJA and RJA correlated more strongly with social-communication ($r$'s=0.673 and 0.758) than sensory-regulatory ($r$'s=0.163 and 0.265) risk. OFA correlated more strongly with sensory-regulatory ($r$=0.47) than social-communication ($r$=0.253) risk. All three constructs correlated positively and significantly ($p<.0001$) with overall risk, with RJA showing the strongest relation ($r$=0.649), followed by IJA ($r$=0.535) and OFA ($r$=0.432). RJA was significantly correlated with attention shifting on the ECBQ ($r$= -0.29, $p<.05$), and demonstrated a trend toward significance for Effortful Control ($r$=-0.22, $p$=0.09). RJA and OFA, were positively and significantly correlated with hyporesponsiveness on the SEQ ($r$=0.35, $p$=.007 and $r$=0.41, $p$=.001, respectively).

Conclusions: We found good internal consistency and convergent validity for three constructs tapping aspects of attention in 12-month-olds on the FYI. RJA and OFA were significantly related to hyporesponsiveness, supporting the idea that early-developing attention processes of engagement, disengagement and orienting to social and nonsocial stimuli may be associated with sensory issues. Future studies could use these attentional profiles to identify risk for ASDs and other developmental disorders, and inform the selection of intervention strategies.

**106.032 32** Profiles of Developmental Level, Adaptive Skills, and Diagnostic Symptoms in Late Preterm, Early Term, and Full Term Toddlers with Autism. C. Klaiman*[1], K. E. Caravella[2] and M. D. Lense[3], (1)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*University of South Carolina*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*

Background: Limited research has examined risk for developmental difficulties, including autism, in infants considered late preterm (34-36 weeks gestation) or early term (37-38 weeks gestation), despite reports of increased morbidity in these groups compared with full term infants (39-40 weeks gestation). A study presented at IMFAR 2013 found that among toddlers with autism, those born during the late preterm period showed reduced symptoms of social affect dysfunction compared with those born after 38 weeks (Caravella et al., 2013). However, it is unknown how autism symptoms compare in individuals born in the early term versus full term or late preterm periods.

Objectives: Characterize developmental profiles and autism symptomatology in toddlers with autism who were born across late preterm, early term, and full term gestational periods.

Methods: Participants included 53 male toddlers with autism (M = 24.46 months, SD = 4.05 months) born during late preterm (n=11), early term (n=12), or full term (n=30) gestational periods. Participants were administered the Autism Diagnostic Observation Schedule (ADOS) and Mullen Scales of Early Learning to assess autism symptomatology and developmental level,

respectively, while adaptive functioning was assessed with the Vineland Adaptive Behavior Scales, 2nd Edition, Survey Form.

Results: Greater gestational age was associated with higher overall autism symptomatology on the ADOS (r=0.282, p=0.041). Specifically, greater gestational age was associated with increased Social Affect symptoms (r=0.314, p=0.022) but not Restricted and Repetitive Behavior symptoms (r=0.023, p = NS). Greater gestational age was associated with reduced Receptive Language abilities (r=-0.320, p=0.019) as assessed with the Mullen. Greater gestational age was associated with lower adaptive skills in the domains of Communication (r=-0.340, p=0.013) and Daily Living Skills (r=-0.383, p=0.005), as well as a marginal association with Socialization abilities (r=-0.237, p=0.088).

Analyses based on group classifications found that toddlers with autism born at early term or full term did not differ in regards to their level of autism symptoms, developmental or adaptive functioning. Toddlers born at late preterm had reduced Social Affect symptoms of autism, greater receptive language abilities, and greater adaptive functioning in the domains of Communication, Daily Living Skills, and Socialization than infants born at full term (Cohen's *d*=0.66-1.18). Toddlers born at late preterm versus early term did not differ in regards to level of autism symptoms or developmental functioning but those born at late preterm demonstrated greater adaptive Communication and Daily Living skills (Cohen's *d*=0.84-1.47).

Conclusions: When examining profiles of toddlers with autism who were born during the late preterm, early term, and full term gestational periods, full term infants showed the greatest degree of autism symptomatology, particularly in regards to Social Affect impairments. A new classification system has been proposed to better capture the morbidity associated with early term births compared to full term births (Sengupta et al., 2013). This initial study suggests that with regards to autism symptomatology and developmental functioning, toddlers with autism who are born at early term do not present differently from those born at full term. Implications for factors affecting autism symptom presentation will be discussed.

**106.033 33** Smiling in Infants with and without ASD during Infant-Caregiver Face-to-Face Interactions. R. K. Sandercock*[1], W. Jones[1], A. Klin[1] and S. Shultz[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

Background: Disrupted social engagement is a core feature of autism spectrum disorders (ASD). Individuals with ASD, even intellectually capable adults, have markedly impaired reciprocal social interaction abilities, displaying reduced eye-contact and difficulty using non-verbal cues. By contrast, typically-developing (TD) infants exhibit remarkable sensitivity to social contingencies present in face-to-face interactions very early in development. By approximately 2 months of age, TD infants are already active participants in dyadic interactions and engage in "social smiling": smiles that are linked to vocalizations and affective changes in caregivers. The emergence of social smiling and sensitivity to contingencies between one's own behavior and the behavior of an interactive partner may mark a pivotal moment in infant development, as success in reciprocal social interaction likely plays a key role in shaping future social and communicative outcomes. Consequently, examining smiling early in life may not only provide an early diagnostic marker of ASD, but may also inform how early deviation from the normative course of social development impacts the unfolding of social deficits characteristic of ASD.

Objectives: This study investigates whether TD infants and infants who later receive a diagnosis of ASD differ in: (1) frequency and duration of smiles; and (2) contextual influences on smiling, namely whether smiles are more likely to be elicited when looking towards versus away from a social partner.

Methods: Three-to-five-month-old TD infants (n=16; mean age = 4.16 months) and infants who later received a diagnosis of ASD (n=13; mean age = 4.08 months) participated in this study. Using eye-tracking technology, we recorded 30-second face-to-face interactions between the infants and their caregivers. Infant facial expressions (including smiling), gaze direction, and caregiver facial expressions and vocalizations were coded as in Lavelli & Fogel (2005). Measures analyzed in the present study include:

(1) the proportion of time infants spent smiling; and (2)

the proportion of time infants spent smiling while gazing towards versus away from their caregivers.

Results: Analyses revealed a marginally significant interaction ($p$ = .07) between diagnostic group and gaze direction while smiling. Follow-up analyses showed that TD infants spent significantly more time smiling when looking at their caregivers' faces than when looking away ($p$ = .004). By contrast, infants with ASD showed no difference in time spent smiling while looking at their caregivers' faces versus looking away ($p$=.629).

Conclusions: Results indicate that smiling in TD infants is modulated by social context, with smiles occurring more frequently when gazing at caregivers. This suggests that smiling in TD infants may reflect emotional engagement *directed towards* a social partner. Conversely, smiling behavior in infants with ASD was not modulated by social context, as they were equally likely to smile when gazing away from and towards their caregivers. These results highlight atypicalities in social smiling, which are likely indicative of an early disruption in typical processes of social development. Future directions include continuing these analyses in a larger sample and examining additional measures of sensitivity to social contingencies during face-to-face interactions.

**106.034 34** The Early Signs of Autism in First Year of Life: Identification of Key Factors Using Artificial Neural Networks.
H. Alonim[1], E. Grossi*[2], I. Liberman[3], G. Schayngesicht[4] and D. Tayar[5], (1)*The Mifne Center and Social Science School, Bar Ilan University*, (2)*Autism Research Unit, Villa Santa Maria Institute*, (3)*Research Authority, Western Galilee Academic College,Bar Ilan University*, (4)*The Mifne Center*, (5)*The Mifne Center and Health Care Unit, Health Ministry*

Background:

In a previous study we have presented an innovative methodology to detect early manifestations of autism, using retrospective analysis of parents' video-recordings of their children's first year of life, filmed before any suspicion concerning defective development arose. Traditional statistics did not allow to handle all the information available due to the high intrinsic non linearity and skewed distribution of symptom frequencies. Similar problems hampered the understanding of natural relationships among factors on study, taking into account simultaneously occurrence, their severity and their precocity in onset.

Objectives: The aim of the study is to assess the natural relationships among variables associated with autism onset.

Methods:

This continued data set is composed on 8 variables displayed in 110 infants (76. % boys and 24% girls between the ages of 3-15 months) who were diagnosed with autism at the age of 2-3 years, using retrospective analysis of video-recordings of the infants' first year of life. In addition, interview questionnaires were distributed to the parents. Variables investigated were: Excessive Passivity; Excessive activity; Lack of reaction to voice or presence; Lack of eye contact; Aversion to touch; Delayed motor development; Accelerated growth of head circumference; Resistance to eating; All variables were objectively measured according to a validated evaluation form scoring.

Artificial Neural Networks (Auto-CM system) were applied to highlight the associations among variables under study. Auto-CM is a special kind of Artificial Neural Network developed at Semeion Research Institute (Rome) and successfully applied in many complex chronic degenerative diseases, able to find out consistent trends and associations among variables creating a semantic connectivity map. The matrix of connections, visualized through minimum spanning tree filter, takes into account nonlinear associations among variables and captures connection schemes among clusters.

Results:

The Semantic Connectivity Map developed by Auto-Cm system showed a meaningful scheme of connections. Lack of eye contact resulted a major node in the graph directly linked with autism spectrum diagnosis and coordinating the other three variables (Lack of reaction to voice o presence; Accelerated growth of head circumference; excessive activity); the other major node resulted to be Lack of reaction to

voice o presence, coordinating the other four variables in study.

Conclusions:

Findings from this study indicate the utility of a data mining approach based on artificial neural networks in depicting complexity of the variables related to early manifestation of autism.

**106.035 35** The Specificity of Atypical Language Development in Infants at-Risk for ASD. G. Righi*[1], E. D. Brooks[2], P. Hashim[2], M. Coffman[3], C. E. Mukerji[1], R. Tillman[1], A. Naples[1], J. Terner[4], R. Travieso[2], D. Steinbacher[2], N. Landi[5], L. Mayes[1], J. A. Persing[2] and J. McPartland[1], (1)*Yale University*, (2)*Yale University School of Medicine*, (3)*Virginia Polytechnic Institute and State University*, (4)*Montefiore Medical Center*, (5)*Haskins Laboratories*

Background:

Language delays and deficits in social communication are characteristic features of Autism Spectrum Disorder (ASD). Recent research has identified early-developing atypical patterns of hemispheric lateralization in response to language stimuli. However, it remains unclear whether atypical hemispheric lateralization is specific to ASD or whether it underlies non-syndrome-specific language delays. In order to examine the specificity of neurophysiological responses to language, we recruited three groups of infants: infants at high-risk for ASD by virtue of having a sibling diagnosed with the disorder, infants at normal-risk for ASD, and infants with non-syndromic craniosynostosis (NCS) and deformational plagiocephaly (DP). Infants with NCS and DP represent an ideal comparison group because these conditions have been associated with atypical language development but not with social communication deficits.

Objectives:

This study compared differences in hemispheric lateralization during a language processing task in in infants at high-risk for ASD relative to those with NCS or DP and infants at normal-risk for ASD. We analyzed the EEG signal in two separate ways: (a) event-related potentials (ERP) and (2) event-related linear coherence between frontal and temporo-parietal regions. These two measures were chosen to obtain information about both localized neural responses (ERP) and synchronized activity across larger networks (linear coherence).

Methods:

We collected data from: 13 infants high-risk for ASD, 20 normal-risk controls, and 23 infants with NCS or DP. EEGs were recorded with a 128 channel HydroCel GSN net during auditory presentations of phonemes. EEG data was analyzed to (a) extract ERPs evoked by phonemes (P150, a positive deflection over left and right anterior scalp between 100 and 300 ms), and (b) to compute linear coherence in the time-frequency domain between frontal and temporo-parietal intrahemispheric sites.

Results:

Preliminary analysis revealed a significant Group by Hemisphere interaction in the P150 ($p = 0.036$). Follow up t-tests revealed significant hemispheric differences in normal-risk infants ($p = 0.043$), but not in high-risk infants ($p = 0.431$) or infants with cranial abnormalities ($p = 0.326$). Prior analyses in a different sample of infants revealed that high-risk infants had overall reduced linear coherence between anterior and posterior sites, compared to normal-risk infants. We expect the patterns of lateralization to parallel the findings of our ERP data, suggesting that atypical language development is associated with lack of hemispheric lateralization. However, we expect our three groups to differ in overall coherence, as overall differences in synchronization might underlie broader deficits.

Conclusions:

Preliminary results show that non-syndrome specific atypical language development is associated with reduced hemispheric lateralization during language processing. We anticipate differences in lateralization to be associated primarily with language delays, whereas we expect overall differences in synchronization of large networks to be indicative of broader deficits. The presence of a non-ASD group with documented language delays will provide critical information regarding the specificity of atypical neural responses to language. Differences between infants at-risk for ASD and infants with cranial abnormalities may shed light on early-

developing neural atypicalities that give rise to the communication deficits documented in ASD.

**106.036 36** The Utility of the First Year Inventory in Evaluating Autism Symptoms at 12 Months in Infants at High Risk for ASD. S. Macari*[1], J. Rowberry[2], D. J. Campbell[1], G. M. Chen[3], J. Koller[4] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Developmental and Behavioral Pediatrics, Mike O'Callaghan Federal Medical Center*, (3)*Christian Academy in Japan*, (4)*Hebrew University of Jerusalem*

**Background:** Younger siblings of children with autism spectrum disorder (ASD) (high-risk siblings, HR) are at higher risk of developing ASD and other developmental problems than those in the general population. Research has suggested that some symptoms of ASD are present in HR siblings at 12 months of age. Screening at this age, however, is complicated by variable autism symptom onset patterns, and especially complex in HR populations because of the substantial numbers of HR infants who do not develop ASD but present with similar symptoms over the second year of life.

**Objectives:** We examined the utility of information gathered at 12 months via parental questionnaire (First Year Inventory; FYI; Baranek et al., 2003) for predicting a later diagnosis of ASD in HR infants at the domain and construct level as well as at the item level.

**Methods:** Participants included 96 families of 12-month-old infants: 71 at HR and 25 at low risk (LR) for ASD. The 61 questions on the FYI comprise two domains (Social Communication and Sensory-Regulatory), each domain consisting of four constructs. At 36 months, the infants were extensively assessed (Mullen, ADOS, Reynell, Vineland) by a team of expert clinicians and classified as having ASD (n=16); other delays, subclinical autism symptoms, or a history of either (HR-ATYP; N=36); or typical development (HR-TYP, n=19; LR-TYP, n=25). Analysis consisted of between-group ANOVAs followed by post-hoc tests and classification tree (CART) analysis of FYI items.

**Results:** The four groups differed on the Social Communication domain ($F(3,92)=5.2$, $p=.002$) and two of its four constructs: Social Orienting and Receptive Communication ($F(3,92)=3.0$, $p=.021$) and Imitation ($F(3,92)=6.0$, $p=.001$). Post-hoc analyses showed that infants with ASD had significantly higher (worse) scores on the Social Communication domain compared to HR-ATYP ($p=.025$, $d=.75$) and LR-TYP ($p=.001$, $d=1.18$) but not HR-TYP infants. The ASD group had significantly higher scores on the Social Orienting/Receptive Communication construct than the LR-TYP ($p=.021$, $d=.91$) group, but not the other HR groups. The ASD group had higher scores on the Imitation construct than the HR-ATYP ($p=.004$, $d=.94$), HR-TYP ($p=.002$, $d=1.17$), and LR-TYP ($p=.002$, $d=1.10$) groups, with large effect sizes for each comparison. There were no between-group differences for the Sensory-Regulatory domain or any of its constructs. The CART analysis revealed that a combination of questions related to recent declines in play and communication and to lack of imitation of vocal sounds correctly predicted almost 2/3 of the children with ASD and 93% of the children without ASD.

**Conclusions**: Our results suggest that parent-reported information about social communication and imitation in 12-month-old infants helps identify infants at highest risk for an ASD among HR siblings. We will also discuss concordance between parent report and clinician observation as a critical issue in the development of screening tools.

**106.037 37** The Potential of an Audio-Based Automated Autism Screen: The Result of a Blind Test Using Third-Party Data. D. Xu*[1], B. Boyd[2], J. A. Richards[3] and J. Gilkerson[1], (1)*University of Colorado*, (2)*University of North Carolina at Chapel Hill*, (3)*LENA Foundation*

Background: Our previous research demonstrated the convenience of collecting naturalistic audio data for autism research using wearable recorders. The developed algorithm for automated data analysis has demonstrated reliability and validity. Naturalistic daylong recordings and automated algorithms capture the characteristic behaviors regarding deficits in different areas of development of children with autism, including social-emotional interaction, language and communication and stereotyped behavior. The efficiency and the effectiveness of this methodology make it a promising tool for autism screen. Our previous effort utilized 1363 in-house recordings with 106 typically developing children (TD), 49 children with language delay not related to autism (LD) and 71 children with autism (ASD) (mainly 15-48 months). The cross-

validation relied on the "leave-one-out" simulation with around 90% equal-sensitivity/specificity.

Objectives: Third-party data are desired for further analysis, validation and improvement. Questions are asked: if the performance can hold for a blind test with third-party data; if the behavior characteristics extracted from audio recordings can show consistency when applied to new data; and if any potential issues or improvements can be identified with blind third-party data. This study intends to answer the questions.

Methods: Daylong audio recordings were collected using wearable LENA recorders. The automated algorithm detected key-child, adults and other environment sounds. The statistics in the sequence of sound categories in a child's recording can reflect how the child interacts with the environment. Even the synchrony between the child and caregivers can be indicated by e.g. the co-vocalization rate between them. Human voice was further processed via phone recognition or sound clustering algorithms, providing frequencies of occurrence for phones, sound clusters and their sequences which are highly correlated with language phonetic and vocal development. Prosodic features such as duration, loudness and pitch are highly related to emotions and other behaviors. More than 100 features were analyzed and modeled to provide the risk score for autism using machine learning approaches. The algorithms were trained with the in-house data, and tested with the third-party data.

Results: The third-party data were from three sources using the same type of recorders. Site-1-data had 59 daylong recordings from 31 children with autism (25-48 months); site-2-data had 125 recordings in preschool environments from 67 children with autism (36-68 months) and site-3-data had 115 daylong recordings from 40 children of typical development (11-22 months). Two methods were tested for autism risk. For Method-1 with the trained cutoff threshold, 88 among 98 ASD children were positive (90% sensitivity) and 38 among 40 TD children were negative (95% specificity); varying the threshold gave 95% equal-sensitivity/specificity. For Method-2 with the trained threshold, 84 among 98 ASD children were positive (86% sensitivity); 36 among 40 TD children were negative (90% specificity); and the equal-sensitivity/specificity was 90%.

Conclusions: The test confirmed the performance of around 90% sensitivity/specificity with the third-party data, showing the great potential of the proposed method. The detailed features extracted from audio recordings are discussed with the relationship to autism screen and are compared among both the in-house data and the third-party data for further improvements.

**106.038 38** Treatment As Usual (TAU) for Preschoolers with Autism: Insight from the Artificial Neural Networks Analyses. A. Narzisi*[1], E. Grossi[2] and F. Muratori[3], (1)*University of Pisa - Stella Maris Scientific Institute*, (2)*Villa Santa Maria Institute*, (3)*Stella Maris Scientific Institute*

**Background:** In Italy TAU is composed of specific treatments performed by child neuropsychiatric services (CNS) and of school inclusion with individual support teacher. The Artificial Neural Networks have never been used in order to study the effects of treatment. Auto-CM is a special kind of Artificial Neural Network able to find out consistent trends and associations among variables creating a semantic connectivity map. The matrix of connections, visualized through minimum spanning tree filter takes into account non linear associations among variables and captures connection schemes among clusters.

**Objectives**: The main aim is to use Auto-CM, a specific Artificial Neural Networks, in order to evaluate the natural relationships among outcome measure in a group preschoolers with autism engaged in a treatment as usual (TAU).

**Methods**: 61 preschoolers with ASD aged between 24 and 48 months were recruited at different centers in Italy. They were evaluated by blind researchers at baseline and after six months using ADOS-G, Griffiths Mental Developmental scales, and Vineland Adaptive Behavior scales. Parents filled out MacArthur Inventory, Social Communication Questionnaire, and Child Behavior Check List. All children were referred to community providers for available interventions.

**Results:** At endpoint, most of the children were still classified as having an ADOS-G classification of ASD. However, 21 (34.2%) passed from Autism to Autism Spectrum and 3 (4.2%) from Autism Spectrum to Non-Spectrum. Treatment effects were obtained for cognitive functioning, language, adaptive behavior, and child behavior, without differences between developmental-oriented and

behavioral-oriented interventions. Parent involvement was a mediator for the best clinical outcome. Baseline low impairments of communication, language comprehension, and gesture were predictors of positive outcome. On the other hand Auto-CM system showed complex relationships between studied outcome variables.

**Conclusions:** Treatment as usual, composed of individual therapy plus school supported inclusion, may be an effective intervention in ASD. Better initial levels of communication in the child and parent involvement during treatment have an important role on positive outcome.

**106.039 39** Video-Guided Self Report of ASD Indicators. R. Landa*[1], S. Warnet[2], K. Boswell[1] and K. Sheperd[1], (1)*Kennedy Krieger Institute*, (2)*New York University*

Background:

Existing ASD screeners have modest sensitivity and positive predictive value and often require follow-up questions or screening. Evidence is emerging that video examples of child development patterns activate parents' evaluative thinking about their child's developmental well-being (Sices et al., 2008). We examined the promise of a video-supported tool to assist parents in recognizing signs of ASD in their child (ASD Video-Guided Self-Report; AVSR).

Objectives:

Evaluate whether the AVSR distinguishes children grouped based on their parents' stated concerns about ASD or prior ASD diagnosis.

Evaluate the sensitivity, specificity, and positive predictive value of the AVSR.

Methods:

This study included four groups of children (ages 12-60 months) based on parent report of concern about the child/prior ASD assessment: No concern (n=32; mean age=30 months); Concern about delay but not ASD (Concern-Other; n=15; mean age 32 months); Suspect ASD but no assessment yet (ASD-Suspected; n=37; mean age=33 months); ASD diagnosis based on prior assessment (ASD-Diagnosed; n=32; mean age 43 months). Group differences were assessed on the AVSR, ADOS, and developmental quotient (Mullen Scales of Early Learning Early Learning Composite). Nonparametric tests with bonferroni corrections were used due to unequal variance and/or unequal distribution of scores across the groups. Receiver Operating Characteristic (ROC) analyses were then conducted to evaluate the sensitivity and specificity of the AVSR in detecting ASDs and to determine an appropriate cut-off for classifying participants as having an ASD or not.

Results:

Kruskal-Wallis one-way analysis of variance by ranks identified significant differences between groups ($p$=0.004) across all AVSR scales, with parents in the No Concern group reporting significantly less impairment on all five AVSR scales than parents in the ASD-Suspected and ASD-Diagnosed groups. Those in the Concern-Other group also reported significantly less impairment than those in the ASD-Diagnosed group with respect to Routine Flexibility and Unusual Movement and reported significantly less impairment than those in both ASD groups on Imagination and Play. Similar analyses also identified significantly higher performance on the Mullen Early Learning Composite in the No Concern group compared to the ASD groups ($H(3)$=45.25, $p$<0.001).

The ROC analyses established a cut-off score of 55 on the AVSR to best classify participants as ASD or Non-ASD (based on ADOS and expert clinical judgment) with the area under the curve at 0.8556. This cut-off produced a high sensitivity (93.3%), specificity (77.8%), and positive predictive value (82.4%). There were no false positives in the No Concern group. One false positive was in the Concern-Other group. Nearly 1/3 of the ASD-Suspected group scored 55 on the AVSR, but were not diagnosed with ASD by the clinical expert. These children met ADOS criteria for ASD and/or had other delays. There was one false negative in each group.

Conclusions:

With video support, parents show a high level of ability to identify whether or not their child is showing ASD symptoms. The AVSR shows promise for use at home or in settings where ASD risk is evaluated in children ages one to five years.

**106.040 40** Visual Social Attention in Infants at Risk for Autism Spectrum Disorders Differs Between Schematic and Live-Action Social Scenes. T. Tsang*[1], M. Dapretto[2], T. Hutman[3],

S. S. Jeste[2] and S. Johnson[3], (1)*University of California, Los Angeles*, (2)*UCLA*, (3)*University of California Los Angeles*

Background: Atypical visual attention to faces is a hallmark of autism spectrum disorders (ASD). Studies of infant siblings of children with ASD have investigated the extent to which this behavior serves as an early marker of the disorder. Atypical spontaneous attention to infant-directed social stimuli has been demonstrated in 6 month-old infants with ASD. Given that difficulties in gaze processing in ASD may stem from an aversion to eye contact, it is possible that altered patterns of visual social attention are a consequence of a model's direct gaze in infant-directed bids. Here, we asked whether visual fixation patterns reliably distinguish infants at risk for ASD under less demanding social contexts.

Objectives: The current study investigates social attention among infants at high and low risk for developing ASD while viewing two classes of dynamic social stimuli. These include schematic and live-action representations of social actors interacting with each other without direct intentions to engage the viewer.

Methods: Six and 9 month old infants [high risk (HR) n = 17; low risk (LR) n = 29] viewed two 2-minute full audiovisual video segments taken from a cartoon (*A Charlie Brown Christmas*) and a children's television program (*Sesame Street*). Videos were matched for duration, action sequences, motion, social interactions, and musical and linguistic content. Eye movements were recorded with a Tobii T60 eye-tracker. ASD diagnoses were rendered using clinical best estimate and DSM criteria when children were 36 months old, assigning the HR-infant siblings into ASD (HR-ASD; N = 7), non-ASD delayed (HR-DD; N =3) and typical outcome groups (HR-TD; N = 7). The principle dependent variable was the proportion of infants' attention to faces in the stimuli.

Results: Attention to faces when viewing the *Charlie Brown* and *Sesame Street* stimuli were similar within HR and LR groups, which did not differ by age. Infants exhibited greater attention to schematic faces than live-action faces (HR: $t(20) = 6.046$, $p < 0.001$; LR: $t(24) = 10.579$, $p < 0.001$). Attention to faces in *Charlie Brown* was similar among HR-ASD, HR-TD and LR infants. HR infants selectively attended less to faces in the *Sesame Street* stimuli than LR infants ($p < 0.01$). Among LR infants, attention to faces in *Charlie Brown* was highly correlated with attention to faces in *Sesame Street* ($p < 0.05$). However, this relation did not hold in the HR group. Attention to faces among the HR-ASD infants was strongly correlated with 24-month ADOS Social Affect scores, ($r = .787$, $p = 0.008$).

Conclusions: The infants exhibited greater visual attention toward schematic depictions of faces than real ones. Our preliminary results suggest that while attenuated attention to realistic social stimuli may be a behavioral endophenotype for ASD, attention to faces *per se* may not be sufficient for predicting outcome in HR-infants. The positive association between level of social impairment and social attention suggests that faces may provide different reward value for infants at risk for ASD. Additional research should further characterize active and passive looking behavior in infants at risk for ASD.

**106.041 41** Who Are Blossomers? Case Studies of Children with Autism Who Blossomed through ABA Parent Training. R. Jamil*[1], M. N. Gragg[1], S. A. Scott[1] and H. E. Hebert[2], (1)*University of Windsor*, (2)*The Summit Centre for Preschool Children With Autism*

**Background**: Research has found that about 10% of children with autism show developmental trajectories known as "bloomers" (Fountain, Winter, & Bearman, 2012) or "improvers" (Gotham, Pickles, & Lord, 2012). These children initially present as low-functioning and show rapid improvement until they later present as high-functioning. Children with autism have been classified in the improving trajectory based on rapid increase in skills (i.e., communication, social, intellectual) or decrease in core autistic symptoms. Despite recent interest in developmental trajectories, there remains a need for in-depth description of children who "blossom," including risk and protective factors and treatment services accessed.

**Objectives**: The initial objective was to identify preschool children with autism who were "blossomers," i.e., made rapid initial progress in cognitive and adaptive skills, in an applied behaviour analysis (ABA) parent training program. A secondary objective was to provide a rich description of the children during their early years and at follow-up, 1 to 5 years later.

**Methods**: Archival data from a three-month ABA parent training program were used to examine the initial progress of 32 children (81% boys) with autism (initial mean age = 41 months; range = 19 to 61 months). Parents most commonly were 35 to 44 years of age; mothers (88%); had some college or post-graduate education and family income of $50K to $75K (Can). The program provided 180 hours of parent training on the principles of ABA and how to implement ABA with their children. Mullen Scales of Early Learning (MSEL) and Vineland Adaptive Behavior Scales – Second Edition (VABS-II) scores from pre- and post-parent training were used to classify the initial progress of the children. "Blossomers" were described in detail through archival data and follow-up. Parents and children were invited back for parent interviews, questionnaires, and an updated intellectual and adaptive assessment.

**Results**: The total group gained an average of 11.30 points in MSEL composite standard scores and 3.22 points in VABS-II composite standard scores over the 3 month program. Preliminary data analysis identified six children who made substantial gains in both MSEL and VABS-II composite standard scores. The "blossomer" group of children showed an average of 19 points gain in MSEL scores (range 9 to 33 points) and 10.33 points gain in VABS-II scores (range 6 to 17 points). Those six children were identified as blossomers and invited for case study follow-up with their parents.

**Conclusions**: Case studies described the characteristics of children who were classified as "blossomers." Archival data on parental stress and burnout levels, parental beliefs in the effectiveness of ABA, parental levels of empowerment and demographic factors such as parental education and socioeconomic status were investigated. Factors explored upon follow-up included the extent parents still use ABA principles; the role of the family support system; parenting qualities; child characteristics, academic supports, peer relationships; and additional interventions. These findings highlight the characteristics of children who advanced from low- to high-functioning, and the individual, family, and system factors involved. Clinical implications are discussed. Data collection is ongoing.

## 107 Epidemiology

**107.042 42** Access to Care for African-American Families Affected By Autism: Pilot of an Event History Calendar Interview. A. Abbacchi*[1], Y. Zhang[1], P. Shattuck[2], D. S. Mandell[3], D. H. Geschwind[4] and J. N. Constantino[1], (1)*Washington University School of Medicine*, (2)*A.J. Drexel Autism Institute, Drexel University*, (3)*University of Pennsylvania School of Medicine*, (4)*UCLA*

**Background:** Diagnostic delays and compromised access to quality health care affect many African American children affected by Autism Spectrum Disorders (ASD). Recent studies have shown higher rates of co-occurring intellectual disability and epilepsy in African-American children diagnosed with an ASD as compared to Caucasian children. **Objectives:** The aim of this research is to develop and validate an instrument capable of ascertaining barriers to care relevant to early identification and treatment of ASD. This study provides initial descriptive data obtained from a newly-developed *Event History Calendar Interview* aimed at characterizing the process and experience of obtaining a diagnosis and accessing services for a child with ASD. **Methods**: Subjects were participants in AUTISM GENETICS, PHASE II: Increasing Representation of Human Diversity, an NICHD Autism Center of Excellent Network focused on gene discovery by accruing a biomaterials collection oversampled for African-American families, who are otherwise grossly under-represented in existing autism gene banks. This report describes validation data from the first 40 interviews of African-American parents with at least one child diagnosed with an ASD. The sample consisted of 34 male and 6 female children, mean age 10.9±4.3, mean IQ=83±15.2. 90% of the children were verbal; 78% of the children were language delayed (mean age single words=28.2±13.8 months; mean age of phrases=44.0±18.0 months). SRS-2 t-scores were calculated by parent-report (mean=75±9.2) and teacher-report (mean=70±10.6). All diagnoses of ASD were confirmed using the ADI-R and/or ADOS and expert clinician diagnosis. **Results:** Mean age of parent's first concerns was 22.1±13.6 months; however average age of an official ASD diagnosis was not until 66.0±32.7 months. 50% of children in this sample were diagnosed with some other disorder before receiving an ASD diagnosis; 50% of those children were initially labeled ADHD. 38% of the sample reported visiting professionals 6 or more times for an evaluation before receiving a diagnosis for their child. Significant difficulties that contributed

to a delay in diagnosis were: wait time to get an appointment (33%); insurance difficulties (23%); time commitment and scheduling difficulties (23%). Median reported income at time of first concerns was $27,500. Parental level of education at time of first concerns and age of first official ASD diagnosis was not significantly correlated (r=.08, p=.63). Mean age special services began was 50.0±23.5 months; all children had received some type of intervention at the time of the interview. In this sample, 15% of children were denied services at some point by the state-based early intervention program or the special school district. With the exception of one family, all had a primary care resource, all children had medical insurance (40% private or employer-based; 60% public, including Medicaid or state-based programs). **Conclusions:** The Event History Calendar Interview Method proved capable of identifying an average delay of 44 months between age of first concern and age of official ASD diagnosis in this minority family sample. This method holds significant potential for feasible identification of specific barriers to care that can be targeted to resolve delays and disparities in diagnosis and treatment for specific populations of children with ASD.

**107.043 43** Agreement Between Multiple Autism Diagnostic Instruments and Clinical Judgment Among Taiwanese Children in the Community. P. C. Tsai*[1], R. A. Harrington[2], I. T. Li[3], C. C. Wu[4], C. H. Tsai[5], C. L. Chu[6], H. Y. Hsu[3], C. L. Chang[7], W. T. Kao[8], C. C. Chien[9], F. W. Lung[10] and L. C. Lee[1], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*Johns Hopkins University*, (3)*Kaohsiung Medical University Chung-Ho Memorial Hospital*, (4)*Department of Psychology, Kaohsiung Medical University*, (5)*Kaohsiung Municipal Kai-Syuan Psychiatric Hospital*, (6)*National Chung Cheng University*, (7)*Graduate Institue of Medicine, Kaohsiung Medical University*, (8)*National Defense Medical Center*, (9)*Kaohsiung Armed Forces General Hospital*, (10)*Taipei City Hospital*

Background: Several diagnostic measures for Autism Spectrum Disorder (ASD) are currently available and widely used in Western countries. Some of these tools are based on information obtained through caregiver/parent interview (e.g., Autism Diagnostic Interview-Revised (ADI-R)), while others are direct observations of the child (e.g., Autism Diagnostic Observation Schedule (ADOS)). While these tools are well-validated for Western populations, their utility and validity are unknown for populations in other international settings. Understanding the agreement between diagnoses derived from these instruments in non-Western populations may provide guidance for diagnosing ASD.

Objectives: This study aims to examine the agreement among multiple diagnostic instruments for ASD (ADOS, ADI-R, and clinical judgment based on DSM-IV criteria) in a community-based study in Taiwan. A secondary purpose is to examine whether combining parent-reported Social Communication Questionnaire (SCQ) and ADOS results improves diagnostic agreement with DSM-IV-based clinical judgment for ASD.

Methods: A community-based epidemiologic study of autism in school children aged 6-8 involving a multi-stage case identification design was conducted in PingTung, Taiwan. The study first screened first and second graders using the SCQ, then invited children who have SCQ>=7 for a clinical visit. At the clinical visit, 27 boys and 19 girls and their primary caregivers completed the ADOS, ADI-R, and were evaluated by local child psychiatrists to determine their DSM-IV-based diagnosis. All study instruments were translated and adapted from English into Chinese Mandarin. DSM-IV-based clinical judgment served as the referent standard. In addition to recommended cut-offs from the ADOS and ADI-R manuals, we defined ADOS-subclinical as having one domain score one point below the ASD cut-off for that domain; whereas ADI-R-subclinical refers to when one domain score does not meet the autism cut-off. Consequently, seven diagnostic criteria were defined to compare against the referent standard: 1) SCQ>=11 and ADOS-ASD, 2) SCQ>=11 and ADOS-ASD or subclinical, 3) SCQ>=15 and ADOS-ASD, 4) SCQ>=15 and ADOS-ASD or subclinical, 5) ADOS-ASD, 6) ADOS-ASD or subclinical, and 7) ADI-R autism or subclinical.

Results: Based on the child psychiatrists' diagnoses, there were 7 children with ASD, 24 with other developmental disabilities (DD), and 15 unaffected with ASD or other DD. The criteria of SCQ>=15 and ADOS-ASD yielded the highest agreement with the gold standard (84%), with 4.3% false positive and 10.9% false negative, followed by SCQ>=15 and ADOS-ASD/subclinical (80% agreement, 13.3% false positive, and 6.7% false negative). ADOS-ASD/subclinical bore the lowest agreement, 60.9%, due to a high percentage of false positives (34.8%).

Conclusions: These findings support the inclusion of both parent-reported information (e.g. SCQ) and direct observation of the child (e.g. ADOS) in determining ASD diagnoses. The ADOS intends to provide an objective observation of the child, however, when used alone with its standard criteria, it is prone to false positives. The ADI-R is time consuming and sensitive to caregivers' cultural backgrounds and subjective interpretation. In settings where diagnosticians and expert clinicians are not available, or where cultural backgrounds are substantially different from where the tool was developed, combining the ADOS with parent-reported SCQ can be considered as a way to diagnose ASD.

**107.044 44** Are Males and Females with ASD More Similar Than We Thought?. J. L. Mussey*[1], N. C. Ginn[1], M. R. Klinger[2] and L. G. Klinger[1], (1)*University of North Carolina*, (2)*University of North Carolina - Chapel Hill*

Background:

The predominance of autism spectrum disorder (ASD) diagnoses among males, with average estimates suggesting a 4:1 ratio (Baird et al., 2006), is one of the most consistent features of the disorder. Previous research examining gender differences among individuals with ASD has suggested that females with this disorder have lower IQ associated with greater symptom impairment (Fombonne, 2009). However, past gender research has been limited by inconsistent findings, small female sample sizes, reliance on parent report measures, and confounding variables such as age and intelligence (Kirkovski, Enticott, & Fitzgerald, 2013).

Objectives:

The purpose of this study was to examine gender differences in intelligence, age of diagnosis, and symptom severity in a community-based clinic sample. This study attempted to overcome past methodological limitations by using a large sample of females and clinician report measures.

Methods:

Evaluations were conducted across statewide outpatient clinics operated by the University of North Carolina TEACCH Autism Program between January 2001 and March 2013. A total of 679 participants (males=566, females=113) who provided consent for their clinical data to be used for research purposes were selected for analysis. These participants were administered an ADOS, CARS, and an IQ measure and received a DSM-IV clinical diagnosis of Autistic Disorder, Asperger's Syndrome, or PDD-NOS. Approximately 24% of the sample had an IQ score below 70 (M=85.9), 17% of the sample was female, and the age at time of diagnosis ranged from 5 years, 0 months to 56 years, 4 months.

Results:

When controlling for IQ and age at diagnosis, there was a very small, yet significant, effect of gender on total CARS score, $B = .07$, $t(675) = 2.05$, $p = .04$. Females had an average total CARS score that was 0.92 points higher than for males. When controlling for the effect of IQ and age at diagnosis, there was no effect of gender , $B = .06$, $t(675) = 1.64$, $p = .10$. Overall, there were no gender differences in IQ scores, $t(677) = .17$, $p = .86$, or age at time of diagnosis, $t(677) = .61$, $p = .54$.

Conclusions:

Overall, these results suggest either very small or no gender differences in IQ, age at diagnosis, or symptom severity. There is a slight difference with females having higher average total scores on the CARS, but this difference is likely of minimal clinical significance based on its extremely small effect size. As this is a large sample representative of a clinical population of individuals diagnosed with ASD, it has substantial power to find potential differences while also taking into account IQ and age of diagnosis factors that have not been consistently controlled for in previous research. These results suggest that gender differences in IQ and ASD symptomatology are likely less important than previously believed.

**107.045 45** Association Between a Polymorphism in the Maternal Serotonin Transporter Gene and Prenatal Stress and a Subset of ASD with Hypersensitivity to Sensory Stimuli. P. Hecht*[1], M. Tilley[2] and D. Q. Beversdorf[1], (1)*University of Missouri*, (2)*Central Methodist University*

Background:

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with a highly heterogeneous phenotype. Identifying subsets of ASD and their possible causes is a critical step in

creating a more complete understanding of the disorder and may provide insight into potential treatments. Dysfunction in the serotonergic system has been implicated in the etiology of ASD. Evidence in animal models and preliminary data in humans in our lab suggests that a maternal polymorphism in the promoter region (5-HTTLPR) of the serotonin transporter gene (SLC6A4) interacts with prenatal stress to cause an increased risk for the development of ASD in the child. Knockout of the serotonin transporter has shown the critical role of this gene in the proper development of the sensory barrel fields in the rodent brain. Since a portion of individuals with ASD have extreme hypersensitivity to sensory stimuli, it is of interest to investigate the possible association between the maternal 5-HTTLPR polymorphism and prenatal stress, both of which have profound effects on the serotonergic system, and this abnormal sensory phenotype in the ASD population.

Objectives:

Our aim is to discover if children with ASD exposed to prenatal stress with a mother carrying the short allele in the promoter region of the serotonin transporter gene are more prone to have hypersensitivity to sensory stimuli.

Methods:

Blood was collected from families with children diagnosed with ASD for genetic analysis. DNA was isolated using a Flexigene (Qiagen, Valencia, CA) kit following manufacturer specifications. PCR was performed using previously documented protocols. Products were then analyzed via gel electrophoresis. Mothers were asked to complete several questionnaires regarding their history of stress exposure during pregnancy, and the timing of the stressors. Additionally, forms describing detailed information on the child's sensitivity to visual and auditory stimuli were filled out by the parents.

Results:

Early evidence suggests that a maternal 44 base-pair deletion in the 5-HTTLPR interacts with prenatal stressors to increase the risk for a subset of ASD with hypersensitivity to sensory stimuli. These children were more likely to be reported as having severe discomfort and negative reactions to either visual or auditory stimuli or both compared to children with ASD not exposed to these factors.

Conclusions:

This study is beginning to suggest a specific gene and environment interaction during development may increase the risk for a particular subset of ASD. More data is needed and is still being collected in this study. However, these preliminary results provide insight into a distinct mechanism underlying a specific behavioral phenotype observed in this neurodevelopmental condition.

**107.046 46** Changes over Time in ASD Prevalence and Characteristics Among Children Aged 3-17 Years, National Health Interview Survey, United States, 1997-2011. A. B. Goodman*, L. H. Tian, C. E. Rice and L. A. Schieve, *Centers for Disease Control and Prevention*

Background: Previous studies suggest a dramatic rise in the estimated prevalence of autism spectrum disorder (ASD) in the past two decades. Further information is needed on whether there have been concomitant changes in the characteristics of children identified with ASD, in order to better understand patterns of identification and potential risk factors among sub-groups of children.

Objectives: To estimate trends in prevalence of ASD among US children aged 3-17 years in 1997-2011 and to describe differences in associations between ASD and selected sociodemographic and birth characteristics in early (1997-2003) versus late (2004-2010) time periods.

Methods: The National Health Interview Survey (NHIS) is an ongoing national survey representing the civilian, non-institutionalized population of the United States. We included children aged 3-17 years in NHIS 1997-2011. A child was considered to have autism if a parent/caregiver answered affirmatively to the question: "Has a doctor or health professional ever told you that [CHILD] had autism?" For the 2011 survey, the term "autism spectrum disorder" replaced "autism". Logistic regression determined associations between autism or ASD and selected characteristics including sex, race/ethnicity, age, maternal education, family income-to-poverty ratio, health insurance, and birth weight. The family income-to-poverty ratio was derived using multiple-

imputation. Analyses accounted for the complex survey design, and data were weighted to provide nationally-representative estimates.

Results:

The estimated prevalence of autism increased from 0.8/1,000 children in 1997 to 10/1,000 in 2010; the prevalence of ASD in 2011 was 12/1,000. For all subgroups examined except black children, prevalence increased more than two-fold between the 1997-2003 and 2004-2010 time periods; in black children, the prevalence increase of 50% did not reach statistical significance.

In both 1997-2003 and 2004-2010, the odds of ASD were significantly higher among: males (versus females, 1997-2003 aOR:3.8(2.4-6.1), 2004-2010 aOR:3.9(2.9-5.3)) and children insured by Medicaid (versus privately insured, 1997-2003 aOR:2.1(1.1-4.1), 2004-2010 aOR:2.0(1.4-2.9)). Although findings were not statistically significant in 1997-2003, in both time periods the odds of ASD were higher among children whose mothers had a college degree (versus no college degree,1997-2003 aOR: 1.6(0.9-2.5), 2004-2010 aOR: 1.5(1.1-2.0)) and children with birth weight >4 kilograms (versus 2.5-4 kilograms, 1997-2003 aOR: 1.2(0.7-2.0), 2004-2010 aOR:1.4(1.1-1.9)). For 2004-2010 only, the odds of ASD were significantly lower among black children (versus white, 1997-2003 aOR: 1.1(0.6-1.8), 2004-2010 aOR:0.5(0.3-0.7)) and Hispanic children (versus white, 1997-2003 aOR: 0.8(0.5-1.2), 2004-2010 aOR:0.4(0.3-0.6)).

Because the autism question changed in 2011, we did not combine these data with the 2004-2010 grouping; nonetheless, preliminary assessment indicates a similar pattern of results for 2011 and 2004-2010.

Conclusions: The prevalence of parent-identified ASD increased more than ten-fold overall from 1997-2010. Similar increases were observed for all sub-groups except black children, who had a smaller increase, possibly indicating a lag in identification. While many characteristics associated with ASD were similar for the 1997-2003 and 2004-2010 time periods, in the later time period only there was a significant differential between children who were white and children who were either black or Hispanic. These data have potential implications for better understanding which population sub-groups might be under-identified and thus, under-served.

**107.047 47** Comparison of Time Spent in Moderate and Vigorous Activity Among Adolescents with Autism Spectrum Disorder and Typically Developing Adolescents. L. G. Bandini*[1], H. Stanish[2], C. Curtin[1], S. Phillips[3], M. C. T. Maslin[1] and A. Must[3], (1)*University of Massachusetts Medical School*, (2)*University of Massachusetts Boston*, (3)*Tufts University School of Medicine*

**Background:** Regular physical activity (PA) is important to overall health and well being. Despite substantial research on PA in typically developing (TD) adolescents, much less is known about the PA level of adolescents with autism spectrum disorder (ASD).

**Objectives:** To compare the frequency of participation in physical activities and time spent in moderate and vigorous activity (MVPA) between adolescents with ASD and TD adolescents. We hypothesized that adolescents with ASD would participate in fewer physical activities and spend less time in MVPA compared to their TD peers.

**Methods:** Thirty-five adolescents with ASD (29 males/6 females) and 60 TD adolescents (36 males/24 females) ages 13-19 (mean age 15.5 years) participated in the Teens Recreational and Activity Choices study. Adolescents were interviewed jointly with their parents about their participation in physical activities over the previous year and were asked to wear an activity monitor (accelerometer) for 5 weekdays and 2 weekend days. The number of different physical activities the adolescent participated in was determined from the joint interview, with regular participation defined as an activity done 12 or more times in the prior year. Time spent in MVPA was determined by accelerometry.

**Results:** Adolescents with ASD participated in significantly fewer 'regular' activities than TD teens, but only among those younger than 16 years of age. After adjustment for sex, for adolescents under 16 years of age, those with ASD participated in 5.3 activities on average, compared to 7.1 activities for TD adolescents (p=0.03). In contrast, after adjustment for sex, for adolescents older than 16 years there was no statistically significant difference between the groups (5.6 vs. 5.7 activities, for ASD vs. TD,

respectively). Walking/hiking and active video gaming were among the top regular activities in both groups. Compared to TD adolescents, adolescents with ASD spent significantly less time in MVPA. After adjustment for age and sex, adolescents with ASD spent approximately 28 minutes of MVPA daily compared to 52 minutes among TD adolescents ($p<0.01$). In addition, we observed a significant group-by-age interaction; when the data were stratified by age and adjusted for sex, we found a significant group difference only among those younger than 16 years (TD=52 minutes/day, ASD=26 minutes/day, $p<0.01$). Among older teens, the pattern was similar but not statistically significant (TD=50 minutes/day, ASD=33 minutes/day, $p=0.16$). Among those subjects who wore an accelerometer, participants in neither of the groups met the recommended 60 minutes of physical activity daily: 29% of TD teens met the recommendation compared to 14% of teens with ASD, although this was not significantly different between groups.

**Conclusions:** We found that teens with ASD who were younger than 16 years of age participated in fewer regular activities and spent significantly less time in MVPA than their same age TD peers. Additionally, most adolescents did not meet the daily recommendations for 60 minutes of MVPA. These findings underscore the need for research on how youth with ASD can be supported to increase their participation in daily MVPA.

**107.048 48** Compromised Indices of Quality of Life Among Parents of Children with Autism Spectrum Disorder in Oman: A Case-Control Study. O. A. Al-Farsi*[1], Y. M. Al-Farsi[1], M. M. Al-Sharbati[1], M. I. Waly[1], M. A. al-Shafaee[2], A. Ouhtit[1], M. M. Al-Khaduri[1], M. F. Al-Said[3] and S. al-Adawi[1], (1)*Sultan Qaboos University*, (2)*S.Q.U.*, (3)*Sultan Qaboos university*

**Background:**

Parents of children with autism spectrum disorder (ASD) usually face many obstacles ranging from psychological to financial difficulties while caring for their children. The consistent exposure to these constrains might negatively affect their quality of life (QOL).

**Objectives:**

To explore indices of QOL among parents caring from children with ASD, compared to parents of non-ASD children.

**Methods:**

A population-based case-control study was conducted among 122 ASD cases. The control groups were composed of 81 parents of children with intellectual disabilities other than ASD, and 90 parents of typically-developed children. A standardized and validated Arabic version of World Health Organization Quality of Life (WHO-QOL) has been used. The indices of QOL were collected over four domains: physical health, psychological well-being, social relationships, and overall environment.

**Results:**

Among parents of children with ASD, the social domain had the highest score (mean= 73), while physical domain had the lowest score (mean= 60.5). Parents of Typically developed children had the highest QOL scores whereas parents with children with ASD the lowest score of QOL. Regarding the assessment of general quality of life, parents with ASD children who considered themselves havinga good QOL were only 42%, compared to 86% and 65% of parents with typically developed and intellectual disabilities children, respectively. The differences in proportions were statistically significant (P-value = 0.03).

**Conclusions:**

The study provides a heuristic evidence that QOL of parents caring for ASD is compromised compared to other parents. The most domain of QOL affected was the physical domain.

**107.049 49** DNA Methylation As a Biomarker for Prenatal Exposures Implicated in Autism Spectrum Disorders. C. Ladd-Acosta*[1], B. K. Lee[2], S. V. Andrews[1], C. J. Newschaffer[2], L. A. Schieve[3], G. C. Windham[4], L. A. Croen[5], A. P. Feinberg[1] and M. D. Fallin[6], (1)*Johns Hopkins University*, (2)*Drexel University School of Public Health*, (3)*Centers for Disease Control and Prevention*, (4)*California Dept of Public Health*, (5)*Kaiser Permanente Northern California*, (6)*Johns Hopkins Bloomberg School of Public Health*

Background: Environmental exposures have recently been shown to play a larger role in autism spectrum disorders (ASD) than previously thought. For example, reports have shown

prenatal exposure to select serotonin reuptake inhibitors (SSRIs) is associated with an increased risk for ASD (Croen *et al.* 2011; Rai *et al.* 2013). However, most population-based autism studies lack appropriate and reliable information on prenatal exposure status, making it difficult to assess and definitively determine the relationship between ASD and exposure status. A molecular signature of prenatal exposures, present during childhood, which could serve as a proxy for prenatal exposure when investigating exposure-disease relationships in lieu of having actual prenatal exposure data would be of great utility. Animal models have shown DNA methylation (DNAm), a type of epigenetic mark, is a useful biomarker of environmental exposure. Here we plan to assess the feasibility of DNAm as a biomarker of 6 specific prenatal exposures that have been implicated in ASD.

Objectives: The purpose of this study is to define DNAm signatures, present in blood during childhood, that are associated with prenatal exposure to smoking, alcohol, maternal infection, folic acid, SSRIs, and B2AR medications.

Methods: Among 611 children (both ASD cases and population controls), aged 3-5 years, enrolled in the Study to Explore Early Development (SEED) we used the Infinium450 BeadChip to measure DNAm at over 485,000 loci. Rigorous quality control measures were implemented, leaving 609 children available for downstream methylation analyses. Prenatal exposure data were collected via telephone interview with the mother. For each exposure examined in this study, we created a dichotomous 'exposed' versus 'unexposed' indicator for each trimester and for pregnancy, as a whole, for our primary analyses. For each exposure, we plan to perform regression analyses, adjusting for blood cell composition estimates, race, and age, to identify novel associations with DNAm. Additionally, for smoking, we have analyzed 26 loci shown to have significant correlation between maternal cotinine levels during pregnancy and DNAm levels at birth (Joubert et al. 2012); thus, we examined the persistence of these DNAm changes into childhood.

Results: Our preliminary analysis indicates the approximate frequencies of maternal active smoking, alcohol, folic acid, B2AR, and SSRI use, as well as infection at any point during pregnancy, are 8%, 12%, 90%, 8%, 8%, and 29%, respectively. Our examination of the 26 smoking associated loci, previously identified in birth samples, revealed striking concordance between the current and the previous study in DNAm changes associated with exposure status. These changes appear to be tobacco specific since the changes in DNAm at these 26 sites were not replicated when we examined prenatal exposure to infection, alcohol, or B2AR or SSRI medications. We are currently performing analyses to define DNAm signatures for all exposures and plan to include any additional findings in our presentation.

Conclusions: We show for the first time that a DNAm signature identified at birth associated with prenatal tobacco exposure persists in 3-5 year old children; thus, demonstrating blood-derived DNAm measurements obtained during childhood can retain signatures of *in utero* exposures.

**107.050 50** Developing UK ASD Research Capacity: Regional and UK ASD Research Databases Include 2500 Children Representative of the UK ASD Population. J. R. Parr*[1], F. Warnell[1], B. George[1], M. Johnson[2] and H. McConachie[2], (1)*Institute of Neuroscience, Newcastle University*, (2)*Institute of Health and Society, Newcastle University*

Background: ASD research often requires large numbers of participants, or participants with uncommon characteristics. To improve recruitment to studies, and enable families to take part in research, we developed two large research databases: the Database of Children with ASD in the North East (Dasl$^{n}$e), which has a population sampling frame, and a national database, the Autism Spectrum Database-UK (ASD-UK).

Objectives: To demonstrate the extent to which the databases include children who are broadly representative of the overall childhood ASD population by presenting:

1. Whether children of parents who consent to join ASD-UK are similar to those who do not want to participate.

2. The similarities and differences between the children included in Dasl$^{n}$e (shown representative of the regional population, McConachie et al., 2009 *Archives of Disease in Childhood*) and the children recruited in the first 30 months to ASD-UK.

Methods: Children with ASD are identified in North East England through local ASD assessment teams, and lists held by education. For ASD-UK, parents are approached through more than 60 Child Health teams. All parents give informed consent, and complete information packs about themselves and their child (or children) with ASD, and siblings. Children's diagnosis data are validated through information obtained from clinicians. Dasl$^{n}$e and ASD-UK have permission to collect a small amount of data about non-consenting families.

Results: After 10 years, Dasl$^{n}$e includes 1400 children – around 55% of children aged 2-18 diagnosed with ASD from the local population. After 30 months' recruitment, 1003 children have been included on ASD-UK.

*Similarities between children/parents who consented to join ASD-UK, and those who did not:* Families who consented to join ASD-UK were very similar to those who reported they did not want to participate (n=184) on the following characteristics: DSM-IV ASD diagnosis, gender (4:1 Male:Female) and Townsend social deprivation score derived from postcode (consent versus refusal difference 0.75 on a 21 point scale).

*Similarities between children recruited to Dasl$^{n}$e and ASD-UK:* There were similar proportions of males and females recruited to each database, and also similar proportions of children with a parent-reported learning disability. Considering DSM-IV ASD diagnosis, children recruited to ASD-UK were more likely to have an ASD diagnosis (62% vs. 50%), and slightly less likely to have an Autism or Asperger syndrome diagnosis. Dasl$^{n}$e children were slightly more likely to attend mainstream school (55% vs. 50%).

Conclusions: Researchers wishing to recruit from ASD-UK and the population-based Dasl$^{n}$e can do so knowing that the two databases are both as representative as possible of the ASD child population.

**107.051 51** Environmental Factors Associated with Autism Spectrum Disorders: A Scoping Review. J. G. de Montigny[1], M. T. Do*[2], M. Ofner[2] and M. Carvalho[2], (1)*University of Ottawa*, (2)*Public Health Agency of Canada*

**Background:**

Autism Spectrum Disorders (ASD) is a major public health concern with the etiology of ASD as it relates to the role of environment remains largely unknown. Over the past few decades, a large body of empirical literature is accruing regarding the role of the environment and ASD. Given the vast literature on this topic, a scoping review was conducted to assess the state of knowledge and identify research gaps relating to the role of the environment and the development of ASD.

**Objectives:**

The specific objective of the scoping review is to identify the environmental exposures of the preconception, prenatal, perinatal, postnatal, neonatal, and early-life periods that may be associated to an increased or reduced risk of autism spectrum disorders.

**Methods:**

The scoping review on ASD-related environmental exposures followed the Arksey and O'Malley's scoping framework. Electronic indexes of MedLine, PsychInfo, and ERIC were used to perform using an *a priori* search strategy. Searches were limited to articles published between January 1, 2003 and July 12, 2013. Articles eligible for inclusion dealt with environmental factors associated with ASD, Pervasive Developmental Disorders (PDD) or its sub-classifications of autism and Asperger's syndrome. Environmental factors include biological (e.g., infections, parental conditions), chemical (e.g., metals, air pollution, pesticides), nutritional (e.g., vitamins, folic acid), and social (e.g., SES, stress). Screened articles were excluded if epidemiological associations referred to co-morbidities, the result of living with an ASD, biochemical pathways not directly related to etiology, animal models or strictly genetic studies.

**Results:**

Between January 2013 and July 2013 there were over 50,000 publications on autism related disorders. Applying environmental factors criteria resulted in 4,844 publications (MedLine: n= 2,542, PsychInfo: n=2,008, ERIC: n=294). After removing duplicates and ineligible studies (e.g., mechanism/pathways), 620 studies were available

for review. Of the studies and reviews published, most were based on environmental chemicals (e.g., air pollution, metals) closely followed by biological (e.g., vaccines, pregnancy complications, parental characteristics, immune abnormalies), and nutritional factors (e.g., vitamins). While the causal role of most environmental risks factors remains unclear, prenatal exposure to air pollutants, particularly from nitrogen oxide, particulate matter, and other air pollutants has been consistently associated with increased risk of ASD.

**Conclusions:**

The large body of literature reflects the interest and potential important role of the environment on the incidence of autism. Results of this scoping review were helpful in assessing the extent, range and nature of research activity to date and will be useful in planning of future directed studies.

**107.052 52** Factorial Structure of Autistic Traits in a Large Sample of Indian Children. A. Rudra*[1], S. Banerjee[2], P. Soni[2], S. Mukerji[2], M. Belmonte[3] and B. Chakrabarti[1], (1)*University of Reading*, (2)*Creating Connections*, (3)*Nottingham Trent University*

Background: The Autism Quotient – child version (AQ-C) is s 50-item parent-report questionnaire that aims to quantify autistic traits in children between the ages of 4 to 11 years of age in the general population (Auyeung et al., 2009). The AQ-C comprises 5 theoretically derived domains: social skills, communication, attention to detail, attention switching and imagination. The factor structure of the AQ-C has been ascertained in Western countries and cultures, and the extent to which these factors may generalise to non-Western cultures remains unclear.

Objectives: To derive the factor structure of AQ-C scores from a sample of 4-11 year old school-going children in Kolkata, India, and to compare this to the factor structure reported by Auyeung et al. 2009 (on a British sample). Additionally, to compare the factor structure of AQ-C as a function of respondent language within the Indian sample (English and Bengali).

Methods: Parent report AQ-C was collected from n=2116 4-11 year old children (mean age=6.4, SD= 1.32) from schools across all socio-economic statuses (government, private, and special schools) in Kolkata. The AQ-C was administered to parents, who filled in the questionnaire in English (n=1635) or Bengali (n= 481). For each respondent language, an initial exploratory factor analysis with principal component analysis and promax rotation was carried out. Factors were identified from a scree plot, and fit to a model in confirmatory factor analysis using IBM SPSS AMOS 19.

Results: For the English version of the AQ-C a 4 factor model provided the best fit (GFI = 0.912, RMSEA= 0.048) and explained 27% of the total variance after rotation. The factors corresponded to social skills, attention to detail, mind reading and imagination, resembling the factor analytic structure reported in the original British sample.The Bengali version of the AQ-C, in contrast, was best fit by a 2-factor model with factors of social skills and attention to detail (GFI = 0.902, RMSEA =0.063), explaining 18% of the total variance. In both 3- and 4-factor models for the Bengali AQ-C, an acceptable GFI (0.88) was obtained after removing items that loaded weakly on the factors.

Conclusions: This provides the first report of the factorial structure of autistic traits in children from a general population sample in India. We observe a similar factor structure for the AQ-C as reported in an Auyeung et al., 2009. Interestingly, the Bengali version of the AQ-C was better fitted by a 2 factor model (similar to the model reported in adults by Hoekstra et al., 2008, and replicated in Valla et al., 2010). Extending this work with a larger and more socioeconomically diverse sample for the Bengali version can test if the observed differences in factor structure between languages is driven by the lower sample size for the Bengali version of the questionnaire, or by other socio-cultural parameters which may in this current sample be confounded with language.

**107.053 53** Fetal-Placental Chorionic Surface Arterial and Venous Vascular Network Structure: Quantitative Arterio-Venous Network Differences in ASD and Controls in the Avon Longitudinal Study of Parents and Children. D. P. Misra*[1], C. M. Salafia[2], T. Girardi[2], C. Platt[3], R. Shah[4] and G. Merz[2], (1)*Wayne State University*, (2)*Institute for Basic Research*, (3)*University of Bristol Hospitals*, (4)*Placental Analytics*

Background: We have speculated that, since related gene families and factors promote and maintain both healthy vascular networks and

healthy neoronal connectivity, that measures of a vascular bed created by the fetal genome (in the placenta) may be correlated with the neurodevelopmental disorder of ASD compared to controls with no diagnosis of developmental disability.

Objectives: To measure the arterial and venous networks on the placental chorionic surface to determine whether netowrk structures vary between ASD cases and a population-derived set of controls.

Methods: Placentas from cases diagnosed with autism/ASD in the Avon Longitudinal Study of Parents and Children were matched with cases without diagnosis of disability. Placentas were processed by a protocol that included photography of the placental chorionic surface, to document chorionic arterial and venous networks. Networks were traced by a dedicated team and over 60 variables related to branch generations, branch points, branching angles, vessel tortuosity and vessel caliber, as well as distance between vessels and from vessels to the chorionic surface perimeter were extracted. Two methods of data reduction assessed arterial and venous network differences between ASD cases and controls: Multiple Adaptive Regression Splines (MARS, Salford Systems, CA, USA) and Principal Components Analysis.

Results: Spline regression found no gender influence on the relationship among individual placental chorionic vessel measures, or the relationship of any of 6 factors extracted by PCA. No difference in chorionic plate vessel factors, arterial or venous, was attributable to infant gender. Factors extracted in ASD were uncorrelated with a similar number of factors extracted from the same variables in the controls and again there was no effect of gender on factor relationships. More arterial variables differed between ASD and controls, at levels of as much as 1-2 orders of magnitude increased significance, as compared to venous variables.

Conclusions: Given these observed differences in ASD placentas compared to controls, new methodology for placental examination may be warranted to better define at risk newborns for ASD. The implications are that the maternal environment or intrinsic fetal genetic regulation may influence the growth of the nutrient supply network of the fetus in the placenta, potentially setting the stage for other environmental stressors to interfere with early neuronal sprouting. Given that a major driving force in branching angiogenesis is oscillation or pulsatility of flow, we hypothesize that potentially the decreased electrical excitability *in vivo* of neurons treated with valproate, a known risk factor for ASD when exposure is in the period in which major chorionic surface vascular networks are laid down, translates in changes in fetal heart rate variability that affect pulsatile flow on the placental surface in early pregnancy. We have found no association of number of branches off the umbilical cord insertion (the earliest developed and thus oldest) portions of the placental chorionic surface vascular networks in either ALSPAC ASD cases as compared to controls There appears to be no ASD- associated effect on the early vasculogenic period of placental vascular organization (<6 weeks gestation), with placental chorionic vessel associations only in later branch generations.

**107.054 54** Investigating the Correlation Between Parental Age at Birth and a Diagnosis of Autism Spectrum Disorder in a Sample of Children with Developmental Delays. P. N. Waselkov*, A. N. Harris, S. E. O'Kelley and K. C. Guest, *University of Alabama at Birmingham*

**Background:** Past findings have shown that older ages of both the mother and father are correlated with a child receiving a diagnosis of an autism spectrum disorder (ASD) (Lampi, et al. 2013). Previous research focuses primarily on comparison of ASD children to a typically developing population (Gardener, Spiegelman, & Buka, 2009).

**Objectives:** The main objective of this study was to examine the relation between parental ages for children with an ASD and for children who have other developmental disorders.

**Methods:** 213 children evaluated for ASD through the UAB Civitan-Sparks Clinics were included in these retrospective analyses. Demographic information was obtained from intake and referral documents and ADOS severity scores, IQ and language scores were gathered as measures of disorder severity. The dataset was split into a Non-ASD final diagnosis group ($n$= 95) and an ASD-final-diagnosis group ($n$= 118). The control group of children in the Non-ASD group was unique from those seen in many similar studies in

that they received other developmental diagnoses.

**Results:** Groups were not different on variables of gender, ethnicity, age in months (Non-ASD group: *M*= 62.67, *SD*= 28.26; ASD group *M*= 56.01, *SD*= 27.20), maternal age in years (Non-ASD group *M*=30.13, *SD*= 6.35; ASD group *M*= 32.018, *SD*= 5.99), paternal age in years (Non-ASD group *M*= 33.22, *SD*= 7.47; ASD group *M*= 33.48, *SD*= 5.86), overall IQ score, and non-verbal IQ score (all *p*'s = ns). Children with ASD obtained poorer language scores across measures. ADOS severity scores were also found to be significantly different between the two groups, $t(211) = -9.39$, $p < 0.01$, as would be expected.

In the Non-ASD group, a positive correlation was found between receptive language score and maternal age, $r(56) = 0.264$, $p < 0.05$, no such correlation was found in the ASD group ($p$ = ns), or for paternal age in either group ($p$ = ns). A positive correlation was also found between maternal age and overall IQ in the ASD group: $r(39) = 0.473$, $p < 0.01$, no such correlation was seen in the Non-ASD group ($p$ = ns), or for paternal age in either group ($p$ = ns).

There was found to be an overall significant positive correlation between final diagnosis and maternal age, $r(203) = 0.15$, $p < 0.05$. This showed that older maternal age is associated with an ASD. No such correlation was found between final diagnosis and paternal age, $r(178) = 0.04$, $p$ = ns.

**Conclusions:** As seen in this sample of ASD versus non-ASD developmentally delayed children, the trend is that for the children with an ASD, the older the mother, the higher the IQ of the child and greater likelihood of ASD diagnosis. This trend was not observed in the non-ASD group. There was also found to be a significant positive correlation between receptive language scores and maternal age in the Non-ASD group that was not observed in the ASD group. Further studies need to be done to examine these relationships and their potential causes in more detail. Further implications will be presented in the poster presentation.

**107.055 55** Metabolic Genes and Blood Lead Concentrations in Jamaican Children with and without Autism Spectrum Disorders.

M. H. Rahbar*[1], M. Samms-Vaughan[2], M. Ardjomand-Hessabi[1], K. A. Loveland[3], A. S. Dickerson[4], J. Bressler[5], S. Shakespeare-Pellington[2], M. L. Grove[5] and E. Boerwinkle[5], (1)*The University of Texas Health Science Center at Houston*, (2)*The University of the West Indies*, (3)*University of Texas Medical School*, (4)*University of Texas Health Science Center at Houston*, (5)*University of Texas School of Public Health at Houston*

**Background**: Autism Spectrum Disorders (ASD) are believed to involve both genetic and environmental factors in their etiology. Long-term exposure to lead has been shown to be associated with several glutathione-S-transferase (GST) family genes including GST mu 1 (*GSTM1*), GST pi 1 (*GSTP1*), and GST theta 1 (*GSTT1*) that play a major role in defense against oxidative stress which is linked to ASD.

**Objectives:** To investigate the association between GST genes and ASD, either directly or through interaction with lead exposure, and to identify factors associated with blood lead concentrations (BLCs) among children in Jamaica.

**Methods:** We conducted a case-control study that enrolled children (age 2-8 years) from December 2009-March 2012. We used standard diagnostic tools to ascertain ASD in children from the Jamaican Autism Database at the University of the West Indies. For each confirmed ASD case, we identified an age- and sex- matched typically developing (TD) child as a control. We also administered a pre-tested questionnaire to assess demographic and socioeconomic information, parental education levels, medical history of children, and potential exposure to lead through parental occupation, home environment and food, with a particular focus on the types and amount of vegetables and seafood consumed by children. At the end of the interview, we collected 2 mL of whole blood from each child, which was analyzed for BLCs. Using a General Linear Model (GLM), based on data from 100 matched pairs, we assessed the association of BLCs with ASD status and sources of exposure to lead. We used multivariable GLM to control for potential confounders and to identify risk factors associated with BLCs. We used Conditional Logistic Regression (CLR) models to assess interaction between BLCs and GST genes in relation to ASD status.

**Results:** Nearly 93.0% of the ASD cases and 99.0% of TD controls were Afro-Caribbean. The mean age of the children in both groups was 69 months. In univariable GLM, we found a

significant ($P < 0.05$) difference between geometric mean BLCs of ASD cases (2.25µg/dL) and TD controls (2.73µg/dL). However, when we controlled for potential confounders including parental education levels, place of child's birth (Kingston vs. other areas), pica (habitually ate mud), consumption of shrimp and whole wheat bread, as well as using pots, pans, and dishes made of Teflon for cooking, there was no significant ($P = 0.38$) difference between adjusted geometric mean BLCs of ASD cases (2.49 µg/dL) and controls (2.79µg/dL). CLR models revealed a lack of significant interaction between BLCs and GST genes in relation to ASD status (all three $P > 0.58$). Additionally, in a separate multivariable GLM, we identified pica, consumption of freshwater fish, shellfish, and whole wheat bread as independent risk factors associated with BLCs in Jamaican children.

**Conclusions:** While our results do not support an association between BLCs and ASD, our data suggest that some Jamaican children may be exposed to lead through sources including consumption of shellfish, fresh water fish, and whole wheat bread. We recommend increasing awareness among parents regarding possible dietary sources of lead in Jamaica.

**107.056 56** Mortality Associated with Autism Spectrum Disorders in a Finnish National Birth Cohort. E. Jokiranta*[1], K. Cheslack-Postava[2], A. Suominen[1], D. Sucksdorff[1], V. Lehti[1], A. S. Brown[3] and A. Sourander[1], (1)*University of Turku*, (2)*Columbia University*, (3)*Columbia College of Physicians and Surgeons*

Background:

Previous studies have reported higher risk of mortality among cases with autism spectrum disorders (ASD) compared with the general population. However, there is a lack of study examining the risk of mortality associated with ASD using matched controls and adjusting for covariates.

Objectives:

To examine the association between mortality and ASD after adjusting for covariates.

Methods:

The cohort includes 4705 children born between 1987 and 2005 who were later diagnosed with childhood autism, Asperger's syndrome or pervasive developmental disorders/ pervasive developmental disorders – not otherwise specified (PDD-NOS). Cases were ascertained from the Finnish Hospital Discharge Register, and each case was matched to four controls by gender, date of birth, place of birth, and residence in Finland. Controls were selected from the Finnish Medical Birth Register. These subjects were followed up for possible mortality until December 31, 2011. Conditional logistic regression models were used to assess the associations between mortality and ASD after controlling for maternal age, maternal and paternal psychiatric history, birth weight and gestational age. In addition, we examined the associations based on the categorization of causes of death (1. natural death, 2. accident, 3. suicide, 4. homicide, 5. unclassified). Because of the small number of deaths in the cohort, adjustment was not done with the causes of death.

Results:

Overall 23 ASD cases (20 males, 3 females) and 50 controls (46 males, 4 females) had died. Prior to adjustment, the risk for mortality in ASD was nearly twofold (OR 1.9, 95 % CI 1.1-3.0, p = 0.016). When adjusted with covariates, the risk slightly decreased (OR 1.7, 95 % CI 0.99-2.8, p = 0.056) and was close to statistical significance. The risk was elevated for natural death (OR 2.7, 95 % CI 0.96-7.6, p = 0.059), accidents (OR 1.9, 95 % CI 0.9-4.1, p = 0.091), and suicides (OR 2.3, 95 % CI 0.9-5.9, p = 0.075) among ASD cases compared with the controls.

Conclusions:

The risk for mortality was increased among subjects diagnosed with ASD. The risk was also elevated for preventable deaths (i.e. accidents and suicides).

**107.057 57** Parental Exposure to Occupational Asthmagens and Risk of Autism Spectrum Disorders in the Study to Explore Early Development. A. B. Singer*[1], G. C. Windham[2], L. A. Croen[3], J. Daniels[4], B. K. Lee[5], D. E. Schendel[6], M. D. Fallin[1] and I. Burstyn[5], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*California Dept of Public Health*, (3)*Kaiser Permanente Northern California*, (4)*UNC Gillings School of Public Health*, (5)*Drexel University School of Public Health*, (6)*Aarhus University*

Background: While there is evidence that prenatal environmental factors may contribute to the development of autism spectrum disorders

(ASDs), few specific environmental factors have been elucidated. Some environmental and occupational exposures can trigger immune responses. Specifically, asthmagens are agents that trigger an asthmatic response, which may activate maternal immune systems. There is evidence that activation of the maternal immune system during pregnancy may be linked with ASDs.

Objectives: We seek to determine if mothers of children with ASD were more likely to be exposed to asthmagens during pregnancy than mothers of children with non-ASD developmental delays or typically developing children.

Methods: We are using data from the Study to Explore Early Development (SEED), a multi-site, case-control study in the United States. During a phone interview mothers were asked about jobs held from 3-months prior to conception until the birth of the child or end of breastfeeding. For each job mothers were asked to report job title, employer, location, job start and end date, hours per week, type of business, and main duties. All reported jobs were coded according to the categories of the International Standard Classification of Occupations (ISCO-88). We used an asthma-specific job exposure matrix (JEM) developed by Kennedy et al. to estimate occupational exposures to asthmagens. For each ISCO job code, the JEM specifies whether or not there is a high probability of asthmagen exposure. We will use logistic regression models to examine the association between maternal asthmagen exposures and ASDs, adjusting for sociodemographic covariates.

Results: Our analysis includes 687 ASD cases, 1056 children with non-ASD developmental disabilities, and 965 general population controls whose mothers answered questions about occupational history during pregnancy. 2033 (75%) participants reported at least one job. The average number of jobs per mother was 1.2 among mothers reporting jobs. Mothers of general population controls were more likely to report a job than mothers of children with ASDs or non-ASD developmental delays. Among mothers reporting a job, 14% were exposed to occupational asthmagens according to the JEM. The findings described here are preliminary. Results comparing asthmagen exposure in the case and control groups will be presented.

Conclusions: Evidence suggests that environmental exposures influence ASD risk. Only a few studies have looked at occupational exposures in relation to ASDs, so we are examining workplace exposure to asthmagens in a large case-control study with detailed phenotypic data on cases.

**107.058 58** Periconceptional Folic Acid-Containing Supplements and LINE-1 DNA Methylation in the Marbles Prospective Study of Autism Spectrum Disorder. R. J. Schmidt*[1], A. M. Iosif[1], J. E. Dienes[1], F. Crary[1], J. M. LaSalle[1] and I. Hertz-Picciotto[2], (1)*University of California at Davis*, (2)*UC Davis*

Background: Epigenetic factors have been shown to contribute to the etiology of autism spectrum disorders (ASD). Dietary methyl-donors such as folate are essential for all biological methylation reactions, and maternal levels could influence DNA methylation profiles in children especially around conception when methylation patterns are erased and reestablished. We hypothesize that DNA methylation, influenced by maternal peri-conceptional methyl-donor intake, affects the child's risk for ASD.

Objectives: In a prospective study of high-risk ASD-affected families, we examined relationships between early prenatal vitamin use and DNA methylation of common LINE-1 repeats as a global epigenetic indicator. In addition, we investigated maternal and child DNA methylation in relation to the child's development of ASD.

Methods: Mothers in the MARBLES (Markers of Autism Risk in Babies: Learning Early Signs) study who have at least one child with ASD, and who became pregnant with another child were included. Global DNA methylation levels were measured by bisulfite conversion and LINE-1 pyrosequencing in DNA extracted from maternal whole blood samples collected during each trimester and at delivery, and the child's cord and peripheral blood . Maternal interviews collected information on prenatal vitamin use and time initiated. The Autism Diagnostic Observation Schedule (ADOS) was conducted on children at the MIND Institute clinic at 24 and 36 months and final clinical diagnoses were made at 36 months.

Results: Taking a prenatal vitamin before or during the first month of pregnancy was not significantly associated with LINE-1 DNA methylation in the mother's blood. Prenatal vitamin use during this time was associated a

trend towards lower LINE-1 DNA methylation in the child's peripheral blood. Meeting ASD criteria on the ADOS at 24 months was associated with significantly higher DNA methylation in cord blood, and significantly lower DNA methylation in the child's peripheral blood. In the subset of children with a final diagnosis (at 36 months), ASD case status of the child was associated with similar findings, with few differences in the maternal blood, and trends toward higher LINE-1 DNA methylation in cord blood and lower LINE-1 DNA methylation in the child's peripheral blood.

Conclusions: These preliminary findings suggest that taking prenatal vitamins before and during the first month of pregnancy could impact the child's LINE-1 DNA methylation levels, which are associated with autism symptomology and potentially ASD diagnosis. Further research is needed to confirm these results as more children reach a final diagnosis. Additional studies will also explore influences of total periconceptional folate intake, folate metabolism genes, and serum folate on child DNA methylation patterns.

**107.059 59** Pre-Existing Differences of Mothers of Children with Autism Spectrum Disorder and/or Intellectual Disability: A Review. J. Fairthorne*, J. Bourke, A. Langridge and H. M. Leonard, *Telethon Institute for Child Health Research*

Background:

Few common traits separate the mothers of children with autism spectrum disorder (autism) and intellectual disability (ID) from mothers in the general population.

Objectives:

- To review research on the pre-existing characteristics which differentiate mothers of children with autism and/or ID of unknown cause from each other and from mothers of children without these disabilities
- To provide a source for research into the determinants of autism and/or ID, including the role of genetic and modifiable risk factors.

Methods:

The papers considered for this review resulted from a search of the Medline, Web of Knowledge, Scopus and Google scholar databases.

Combinations of the search terms associated with autism and ID, the hypothesised aetiologies of autism and ID and terms associated with traits of mothers of children with autism and/or ID were used. Examples from each of the three groups are 'autis*, pervasive development disorder* and intellectual disability', immigra*, migra*, ethnic*, immun*' and 'traits, characteristics, mothers, children'.

A paper was included in the review if:

- It was published in a peer-reviewed journal between 1990 and 2012 inclusive;
- It was a full text article in English;
- It described new research;
- It compared a characteristic of parents or mothers of children with ASD and/or ID with parents or mothers of children without disability or with a population norm;
- It assessed characteristics that were pre-existing and not likely to be a result of caring for a child with ASD and/or ID; and
- It used methods of ascertainment and measurement of the characteristic(s) of interest that were assessed as unlikely to lead to bias.

Results:

Overall, autism was correlated positively with socio-economic status (SES), education and age. By contrast, ID had a negative correlation with each of these variables. A reversal was also apparent with parity where lower parity was associated with the autism group and higher with the ID group. More complex associations were found with immigrant status and ethnicity. With the former, excluding Californian population studies, the children of immigrant mothers consistently were associated with increased rates of autism (particularly autism with ID) and lower rates of Mild or moderate ID (mild ID). A reverse scenario was found in California with a higher proportion of mild ID and a lower proportion of autism in the children of immigrant mothers. With ethnicity and with the exception of Asian mothers, there are lower rates of autism and increased rates of ID in the mothers of ethnic minority groups. Asian mothers exhibited an

opposite trend. Further, compared to the ID group, many more traits were associated with the mothers of children with autism in the three areas related to immunology, mental health, pregnancy/childbirth and behavioural traits. Possible explanations for these findings are discussed.

Conclusions:

Further research in these areas may yield more understanding of the genetic and aetiological aspects of autism and ID. In turn, primary and secondary prevention strategies may be refined and/or developed.

**107.060 60** Prevalence Changes in Autism Spectrum Disorders over an 8-Year Period in South Carolina. W. Jenner*, L. A. Carpenter, L. B. King, J. Charles, H. Specter, A. E. Wahlquist, C. C. Bradley and A. P. Cohen, *Medical University of South Carolina*

Background:

There has been growing awareness of autism spectrum disorders (ASD) as a significant public health concern. Once thought of as a rare developmental disability, service providers report continued increases in ASD. Congress passed legislation in 2000 to provide funding for the Centers for Disease Control and Prevention to establish a network of sites in the United States to report the prevalence of ASD. These sites are called the Autism and Developmental Disabilities Monitoring Network (ADDM). The Medical University of South Carolina (SC ADDM) has been a member of the ADDM network since 2000.

Objectives:

1. To examine changes in ASD prevalence over an 8-year period in South Carolina, a state with significant racial and economic diversity. 2. To explore prevalence changes by gender. 3. To investigate changes in age at first diagnosis of ASD including any changes in community reporting.

Methods:

SC ADDM has conducted population-based multiple-source surveillance for ASD using identical study methodology within the same catchment area since 2000. The SC ADDM method uses chart reviews from clinical, education, and disability board records, followed by expert clinician review to determine surveillance case definition. With multiple agreements from SC state agencies, records for children who are 8 years old are screened for behavior triggers and later reviewed by clinical experts to see if that child meets the requirements for an ASD according to the DSM-IV definition.

Results:

In South Carolina, there was a 76% increase in the prevalence of ASD over an 8-year period. In 2000, ASD prevalence was 6.3 / 1000 or 1 in 159 eight year olds. In 2008 ASD prevalence was 11.1/1000 or 1 in 90. Male to female ratio increased 86%, from 2.8 to 1 to 5.2 to 1. The largest increase in ASD prevalence was in males from 9.3/1000 to 19.5/1000. Girls stayed approximately the same, 3.3 to 4.0 / 1000. The median age of first diagnosis of ASD found in any record was 54 months in 2000 and again was 54 months in 2008. In 2000, ASD was recognized in 35% of all ASD records reviewed. Eight years latter ASD was recognized in 63% of ASD records, indicating an increase in the diagnostic rate in available records.

Conclusions:

SC ADDM found 135 more children in an 8-year time span in exactly the same SC geographical region, using identical methodology in each study year. This is an 87% increase, when the population of 8-year olds actually decreased approximately 7% during this time. The increase in case finding is primarily due to the increased number of identified males. Despite increased emphasis on early detection, the average age of first diagnosis remained 4 years, 6 months across study years, leading to missed opportunities for autism specific early intervention. Despite this, there was a significant increase in the recognition of the characteristics of ASD found in clinical records.

**107.061 61** Psychological Burden on Parents of Children with Autism in Oman: A Case Control Study. O. A. Al-Farsi*[1], Y. M. Al-Farsi[1], M. M. Al-Sharbati[1], M. I. Waly[1], M. A. al-Shafaee[2], A. Ouhtit[1], M. M. Al-Khaduri[1], M. F. Al-Said[3] and S. al-Adawi[1], (1)*Sultan Qaboos University*, (2)*S.Q.U.*, (3)*Sultan Qaboos university*

**Background:**

Caregivers of children with ASD may be prone to different psychological disequilibrium such as stress, anxiety, depression, grief, fatigue that affect their behavior and social relationships. Few studies have attempted to quantify the psychological burden on caregivers manifested as feeling with embarrassment, overload, resentment, social isolation, and loss of control**.**

**Objectives:**

The aim of this study is to evaluate the severity of psychological burden among parents of children with autism in Oman compared with parents of non-ASD children.

**Methods:**

A population-based case-control study was conducted among parents of 122 cases of children with ASD and 122 non-ASD controls. The controls were matched on age, gender, ethnicity, and place of residence. A standardized and validated Arabic version of The Zarit Burden Interview (ZBI-22) has been used to evaluate the level of burden among cases and controls.

**Results:**

Overall, the mean ZBI-22 score of psychological burden among parents of children with ASD was 42.9 (SD = 17.6) which was significantly higher than that among parents of control group (26; SD= 10.8), P-value = 0.04. Among cases, 17% of parents suffered from severe psychological burden compared to none (0%) among controls. A substantial proportion of cases (31%) reported moderate psychological burden compared to only 12% among controls, and the difference was statistically significant (P= 0.01). Among cases, mothers reported a higher mean ZBI-22 score compared to fathers (49.7 vs. 35.5), and the proportion of mothers who suffered from severe burden was significantly higher than that among fathers (29% vs. 5%; P-value = 0.001).

**Conclusions:**

The study provides a suggestive evidence that the psychological burden on parents caring for children with ASD is substantial, especially among mothers. The study calls for considering provision of psychological support to parents as an essential component of holistic approach of management of cases of ASD children.

**107.062 62** Psychotropic Medication Use Among Children with and without Autism Spectrum Disorders in 2010. J. M. Madden*[1], M. D. Lakoma[1], V. M. Yau[2], F. L. Lynch[3], D. Rusinak[1], A. A. Owen-Smith[4], K. J. Coleman[5], V. P. Quinn[5] and L. A. Croen[2], (1)*Harvard Medical School and Harvard Pilgrim Health Care Institute*, (2)*Kaiser Permanente Northern California*, (3)*Kaiser Permanente Northwest*, (4)*Kaiser Permanente Georgia*, (5)*Kaiser Permanente Southern California*

Background:

Autism diagnoses have increased alarmingly in recent decades. No known medications can cure the underlying disorder, but a range of psychotropic medications are used to alleviate associated symptoms and behaviors. There is a lack of recent data on use in large pediatric populations.

Objectives:

We examined psychotropic medication use among children with autism spectrum disorders (ASD) in 5 geographically diverse nonprofit US health plans, comparing results to a matched population without ASD. We describe prevalence and intensity of use by therapeutic class, age, gender, diagnostic severity (autistic disorder vs other ASD), and psychiatric comorbidity.

Methods:

All subjects were continuous members in 2009-2010. ASD status (N=8,363) required 2 separate ICD-9 diagnoses in claims 2009-2010; age- and gender-matched peers had no ASD diagnoses in 2009-2010 (N=83,575). We determined comorbidities with a single diagnosis in either year. We analyzed psychiatric drug utilization in 2010 among children aged 1-17, the relative odds of psychotropic treatment associated with ASD status, predictors of use among ASD patients, and frequencies of specific therapeutic combinations and entities.

Results:

Most children with ASD (73.3%) and 17.3% of non-ASD children had other psychiatric diagnoses. Among children with ASD, 46.3% received a psychiatric medication in 2010, compared to 7.4% of non-ASD children; the odds of use were 11.7 higher among children with ASD. Stimulants (21.6%), antipsychotics (19.6%), and antidepressants (17.0%) were the

most commonly used psychiatric drug therapies among children with ASD. Among users for these 3 classes, the average annual supply dispensed ranged from 11.5 months to 9.5 months, respectively. Psychotropic treatment was consistently far more prevalent among children with ASD, whether or not a relevant comorbidity diagnosis was present.

Conclusions:

The intensive use of psychotropics we observed is consistent with earlier reports and highlights the complexity of treatment for children with autism. Nevertheless, published evidence supporting the effectiveness of these treatments in ASD remains scarce. Substantial additional research investment in evaluating the use of psychotropics for ASD is justified by high rates of use in the community.

**107.063 63** Quantifying Change: The Significant Increase of Autism Spectrum Disorder Prevalence in a Rural Population. L. B. King*, J. Charles, J. S. Nicholas, W. Jenner and L. A. Carpenter, *Medical University of South Carolina*

**Background:** The prevalence of Autism Spectrum Disorder (ASD) is now 1 in 88, a 78% increase over the past six years. Efforts are being made to quantify this change.

Previous studies have found a significant urban-rural difference in the prevalence of psychological and other mental disorders. Yet little data on geographic differences has been collected on ASD. A recent study in the UK found that the rate of ASD was higher in the rural population (Kiani), but a study from Taiwan showed that the incidence of ASD was higher in urban areas (Lai). Due to these conflicting reports and different locations, it is imperative that we determine the relationship between ASD and geographical classification so that we may better allocate resources for diagnosis and follow-up care.

**Objectives:** Using the Bureau of the Census definition of a rural area (any incorporated place or census designated place with fewer than 2500 inhabitants that is located outside an urban area), we will determine the rate of change for children meeting criteria for ASD from the South Carolina Autism and Developmental Disabilities Monitoring Program (SC ADDM) in an urban versus rural setting.

**Methods:** Data for this study came from SC ADDM (43% rural in 2000 and 37% rural in 2008). ADDM is a collaborative agreement between 14 sites and the Centers for Disease Control to conduct ASD surveillance in the United States. Data includes all 8-year-old children with an ASD who lived in one of 21 counties in the Coastal and Pee Dee regions of South Carolina in 2000 or 2008 and who were designated as having ASD based on record review. ASD status was determined through extensive screening and records abstraction at multiple educational and clinical sites, followed by expert clinician review and final case determination. This multi-site population-based approach has been used since 2000 and has collected data on 5 cohorts of data (children born in 1992, 1994, 1996, 1998, and 2000). Prevalence will be compared for rural and urban areas and assessed over time to determine whether an increase in rural prevalence is responsible for any of the increase in prevalence seen over the past 6 years. Chi-square tests for differences in two independent proportions will be used to determine significance of changes in the proportion of children with ASD in rural and urban areas.

**Results:** In urban SC, prevalence increased 57% from 7 per 1,000 in 2000 to 11 per 1,000 in 2008 ($x^2$=14.6, p=0.0001). In rural SC, prevalence increased 137% from 5.8 per 1,000 in 2000 to 13.7 per 1,000 ($x^2$=32.5, p<0.0001).

**Conclusions**: The current increases in ASD prevalence in South Carolina can partly be attributed to increases within rural areas. Awareness and outreach throughout the state are possible reasons. Expansion of the current analysis to more ADDM states will focus on quantification of the amount of prevalence increase due to rural prevalence increases.

**107.064 64** Sex Difference in Diagnosis Retention of an Autism Spectrum Disorder (ASD). Y. T. Wu*[1], M. J. Maenner[2], L. D. Wiggins[3], C. E. Rice[4], C. C. Bradley[5], M. L. Lopez[6], R. S. Kirby[7] and L. C. Lee[1], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*US Centers for Disease Control and Prevention*, (3)*Centers for Disease Control and Prevention*, (4)*National Center on Birth Defects and Developmental Disabilities*, (5)*Medical University of South Carolina*, (6)*University of Arkansas for Medical Sciences*, (7)*University of South Florida*

Background: Research findings suggest that although most children retain an ASD diagnosis

after the initial diagnosis, some children may experience sufficient change in symptoms such that they no longer meet criteria for an ASD diagnosis at a later time.

Objectives: To examine whether there is a sex difference in retention of ASD diagnosis and the factors that contribute to ruling out an earlier ASD diagnosis.

Methods: This study utilized data from the Autism and Developmental Disabilities Monitoring Network, a population-based ASD surveillance system for 8-year-old children living in 14 US communities in 2008. 7,077 males and 1,487 females had an ASD diagnosis documented in their school or health records. ASD diagnosis retention status was determined by reviewing whether an ASD diagnosis was later ruled out by a community professional following a documented ASD diagnosis. Children were defined as either retaining an ASD diagnosis (ASD-R) or not retaining an ASD diagnosis (ASD-NR) if a community professional ruled-out an ASD after the date of first documented ASD diagnosis. Multivariable logistic regression was used to examine associations between the co-occurring conditions and diagnosis retention status in males and females.

Results: Most children retained their ASD diagnosis (91% of both males and females). For those who did not, the diagnosis retention time was shorter for males than for females. Some factors, such as diagnosing professional and type of concurrent diagnoses, were differentially associated with diagnosis retention in boys and girls. Factors similarly associated with ASD diagnosis retention in males and females were meeting the ASD surveillance definition, having a higher degree of impairment associated with ASD, and having fewer co-occurring developmental and psychiatric diagnoses. After adjusting for child race, source of surveillance record, and surveillance year, both intellectual disability and sensory integration disorder were associated with ASD-NR in males, whereas developmental disability (DD)-personal/social was associated with ASD-NR in females. Furthermore, both males and females who had co-occurring developmental delays in motor areas or overall, language disorder, Attention-Deficit/Hyperactivity Disorder, learning disability, or any co-occurring developmental diagnosis were more likely to be ASD-NR. Children with co-occurring Oppositional Defiant, anxiety, or mood disorder, or any psychiatric diagnosis were more likely to be classified as ASD-NR than their counterparts without these conditions - this was true in males and in females. Diagnoses of Obsessive-Compulsive or bipolar disorder were associated with ASD-NR in males, but not in females. Hearing loss was associated with ASD-NR in males, whereas epilepsy or any co-occurring neurological diagnoses were associated with ASD-NR in females.

Conclusions: While most children retained their ASD diagnosis through age 8, child sex plays a role in specific characteristics associated with the ASD diagnostic trajectory documented by community professionals. Milder ASD impairment and greater numbers of co-occurring conditions may complicate the diagnostic picture, leading to increased likelihood of an ASD diagnosis eventually being ruled out. Our findings highlight the need for clinicians to be aware of potential challenges with differential ASD diagnosis and co-occurring conditions that may challenge an appropriate diagnosis of ASD for boys and girls at young ages.

**107.065 65** The Likelihood of a Child Developing Autism Spectrum Disorder, Intellectual Disability or Both Is Related to a Mother's Mental Health Status in the Years before the Birth. J. Fairthorne*[1], J. L. Bourke[2], G. Hammond[1], N. De Klerk[1] and H. M. Leonard[1], (1)*Telethon Institute for Child Health Research*, (2)*Telethon Institue for Child Health Research*

Background:

Mothers of children with intellectual disability (ID) and/or autism spectrum disorder (autism) have a higher rate of psychiatric disorders than other mothers. It is not known whether these mothers have a higher rate before the birth of their child with a disability or if the increased rate is due to the increased burden of caring.

Objectives:

To examine whether the existence, and rate by diagnostic category, of maternal out-patient mental health contacts before the birth affected the probability of a child with ID, autism, or both.

Methods:

We linked three Western Australian population-based registers. Case mothers were grouped

according to the disability of the eldest child with a disability (the index child). The comparator group was mothers of children with no autism or ID and here, the index child was their eldest child. We grouped the outpatient contacts into eight diagnostic categories. The effects of the existence of a contact and the rate of contact for a diagnostic group, before the index birth, on subsequent child disability, were examined using multinomial logistic regression.

Results:

Women with an outpatient contact before the index birth were more likely to have a child with mild ID [OR 2.23(1.99, 2.50)], autism with ID [OR 1.83(1.37, 2.44)], autism without ID [OR 2.56(1.85, 3.55) or 'other biomedical ID' [2.19 (1.65, 2.91)]. Previous contacts for developmental disorders increased the odds of having a child with mild ID by 2.09 per contact/ year with 95% CI (1.33, 3.28) and the odds of autism with ID by 1.77 per contact/ year with 95% CI (1.02, 3.08). Previous contacts for childhood and adolescent disorders also increased odds of having a child with mild ID by 1.21 per contact/ year with 95% CI (1.11, 1.32).

Conclusions:

The likelihood of a child with ID, autism or both increased for women with pre-existing mental health contacts. Moreover, the risk of a child with ID was similar to that of autism.

**107.066 66** The National Autism Spectrum-Disorders Surveillance (NASS) System in Canada: Design and Implementation. L. Mery[1], M. Ofner[1], M. Cardinal[1], A. J. Bailey[2], A. M. Ugnat[1] and M. T. Do*[1], (1)*Public Health Agency of Canada*, (2)*UBC*

**Background:**

Across Canada, responding to Autism Spectrum Disorders (ASD) has become of increasing importance to health, education and social service sectors. In recognition of this need, the Public Health Agency of Canada (the Agency) has received a mandate to conduct nationwide surveillance of ASD to ascertain important descriptive and epidemiologically information by 2016. To this end, the Agency has been actively engaging with key stakeholders in this field to develop and implement a **N**ational **A**utism **S**pectrum-Disorders **S**urveillance (NASS) System in Canada.

**Objectives:**

The overall objective of the NASS is to coordinate efforts in filling critical public health knowledge gaps and contribute to advancing a strong evidence base to help improve the lives of those living with ASD in Canada. The NASS will be responsible for ongoing collection, integration, analysis, interpretation and dissemination of data for the reporting of ASD prevalence, characteristics, and related outcomes; both over time and across geographic regions. The specific objective of this presentation is to share and obtain feedback of the progress to date relating to the development and implementation of the NASS.

**Methods:**

To help guide the development and implementation of NASS, the Agency established the Autism Spectrum Disorders Advisory Committee to advise on the most effective approaches to capture data cross Canada. In addition, technical expertise was also sought from the Surveillance Working Group convened to support the operationalization of the process. Based on earlier work through environmental scans of existing data sources across the country, the NASS will use data sources from both the health and education sectors. To date, a public health surveillance case definition for ASD has been established along with the minimum, preferred, and enhanced data elements. Implementation will use a phased approach to provide participating jurisdictions flexibility through Collaborative Surveillance Agreements. The design of the NASS program has been structured into three areas: provincial/territorial implementation, national coordination, and applied analysis.

**Results:**

As part of the implementation phase, *Letters of Invitation*have been sent to all 13 provinces and territories in Canada requesting their participation. These 13 jurisdictions are responsible for the delivery of public health care in Canada. The plan will clearly express program requirements such as the minimal data set, methods of data transfer, use of data for reports, criteria and methods for the approval process (developing the scope of what may be included,

applicable partners, timing, and approximate budget), roles and responsibilities. A set of national indicators and data quality framework is also being created.

**Conclusions:**

A plan for the development of a national surveillance system of ASD for Canada has now been created. The plan is currently implemented with the goal of a first preliminary report to be generated by 2016. Feedback from experts is critical in the continued development of the NASS both within Canada and internationally.

**107.067 67** Understanding Associated Features of Autism Spectrum Disorder and Their Relationship to DSM Diagnostic Criteria. L. D. Wiggins*[1], L. H. Tian[1], K. Van Naarden Braun[1], J. Baio[1], L. A. Schieve[1], M. Maenner[1], H. Clayton[1], M. DiRienzo[2], A. B. Goodman[1] and M. Yeargin-Allsopp[1], (1)*Centers for Disease Control and Prevention*, (2)*Carter Consulting for the Centers for Disease Control and Prevention*

Background:

Children with autism spectrum disorder (ASD) have many features beyond diagnostic symptoms that contribute to phenotypic heterogeneity. Little is known about the underlying structure of these associated features (AF) and how they relate to diagnostic criteria.

Objectives:

Our goal was to examine the latent structure of common ASD AF and the associations between those features and DSM-IV-TR diagnostic symptoms and domains.

Methods:

Children were identified from the Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP). MADDSP is a population-based surveillance system that monitors the prevalence of ASD and other developmental disabilities in metropolitan Atlanta, GA. We included data from the two most recent surveillance years: 2006 and 2008.

Case-finding in MADDSP is based on detailed abstraction of evaluation reports noted in special education and health records. Abstracted information is concatenated and then reviewed by trained clinicians who apply a standardized coding scheme based on DSM-IV-TR criteria to determine ASD case status. Clinician reviewers also code whether each child has any of 13 ASD AF: eating/drinking difficulties, sleeping difficulties, mood difficulties, uneven cognitive skills, aggressive behaviors, oppositional behaviors, delayed motor skills, Attention-Deficit/Hyperactivity Disorder (ADHD) characteristics, unusual fear response, unusual sensory response, self-injurious behaviors, seizures or seizure-like behaviors, and temper tantrums. Latent class analysis was used to classify the structure of the AF.

Results:

1,075 children met the MADDSP ASD surveillance definition, of which 84.3% were males and 55.8% had a co-occurring intellectual disability. The sample was 40.6% Non-Hispanic white, 40.5% Non-Hispanic black, 7.9% Hispanic, 9.2% other or non-specified race, and 1.8% missing race.

The AF most commonly reported were ADHD characteristics (90.4%), mood difficulties (78.5%), and unusual sensory response (75.7%). Three latent classes were distinguished by the probability of having each AF: Class 1 (high probability; 39%) had the highest probability followed by Class 2 (medium probability; 46%) and Class 3 (low probability; 15%). The only exception to this pattern was that Class 1 and Class 2 had an equally high probability of ADHD characteristics. The mean number of AF was 9.7 for Class 1, 6.8 for Class 2, and 3.2 for Class 3 when children were assigned to classes based on posterior probabilities.

Unusual sensory response and temper tantrums were associated with all 12 DSM-IV-TR symptoms from among all three diagnostic domains. Eating/drinking difficulties, mood difficulties, ADHD characteristics, and unusual fear response were each associated with nine DSM-IV-TR symptoms from among all three diagnostic domains. The association between other AF and diagnostic symptoms varied.

Conclusions:

Children with ASD have many AF that can be classified as high, medium, and low in probability. The presence of AF may complicate diagnostic and treatment decisions and should thus be considered when working with children with ASD

(Close et al., 2011). ADHD characteristics, mood difficulties, and unusual sensory response were most prominent in our sample and associated with a majority of ASD diagnostic symptoms. These results support the DSM-V decision to allow dual ADHD and ASD diagnoses and highlight the need for future research on the overlap between ASD, ADHD, and mood and sensory disorders.

**107.068 68** What Can State-Birth Records Contribute to Our Understanding of ASD Risk?. R. C. Urbano*[1], A. Vehorn[2] and Z. Warren[3], (1)*Vanderbilt Kennedy Center*, (2)*TRIAD, Vanderbilt Kennedy Center*, (3)*Vanderbilt University*

Background: Autism Spectrum Disorder (ASD) is thought to be the most heritable of all neurodevelopmental and psychiatric disorders (Abrahams & Geschwind, 2008; O'Roak & State, 2008). However, identification of specific genetic risk variants has proved to be a challenging endeavor and many researchers are now suggesting that there may be multiple pathways to this disorder, including prenatal and postnatal insult (Geschwind & Levitt, 2007). Further investigations into well phenotyped samples are needed in order to help elucidate medical and environmental factors that may contribute to ASD risk.

Objectives: The purpose of this study was to link patients within a local, well phenotyped ASD registry (N=1647) at a large university in the mid-south to official state birth records in order to examine early factors potentially associated with ASD risk. These birth records contain approximately 140 variables pertaining to infant, parent and prenatal health practices.

Methods: Multiple personal identifiers (e.g. names, DOB's, addresses) were used to match ASD registry with birth records. Birth records matched on DOB-year, DOB-month, gender and zip code were selected for the control (N=2200).

Results: Several significant (all p's =< .05) univariate comparisons of child, parent, prenatal practice and reproductive history variables were identified. The ASD group differed from the control group on the following variables: higher APGAR scores (8.8 v 8.7), shorter gestational age (38.1 v 38.4), increased interval between births (54.9 v 48.9 months), started prenatal care earlier (month 2.7 v 2.9), older maternal age (28.5 v 27.0), less use of antibiotics (25.5% v 24.1%), more birth complications (80.2% v 69.4%), fewer obstetrical procedures (26.9% v 37.2%), fewer vaginal deliveries (55.5% v 65.7%), more transfusions (.5% v .01%), more white (89.6% v 83.9%), fewer Hispanic (5.5% v 11.4%), more with advanced education (college or more) (68.4% v 55.3%), and more were married (73.7% v 69.4%). Since the variables in the univariate comparisons are correlated to a greater or lesser degree, a logistic regression analysis comparing the ASD and the control group was completed. The logistic regression confirmed the significant independent contribution of gestational age, inter-pregnancy interval, month care began, antibiotic administration, and maternal ethnicity.

Conclusions: Although several findings represent replications of previous findings (i.e., gestational age, maternal age, fewer vaginal deliveries) several findings are in conflict with previous reports (i.e., higher APGAR scores, increased interval between births, less use of antibiotics). Associations between ASD and non-ASD characteristics documented within medical birth records may help us better understand factors potentially associated with ASD risk. However, such methodologies need to demonstrate replication across samples and be linked to scientific enterprise that can move from association to actual understanding of true risk and risk pathways.

## 108 Intellectual and Behavioral Assessment and Measurement

**108.069 69** Assessment of Change in Autism: Inter-Rater Reliability of Developmental Disabilities CGAS and the OSU Autism CGI. N. Choque Olsson* and S. Bolte, *Karolinska Institutet*

Background: Research on outcome and treatment response (change) in autism spectrum disorder (ASD) is of paramount importance, but the literature on these issues is only slowly improving. One reason is the lack evaluated economic tools to assess change in autism. Despite the general widespread use the Children's Global Assessment Scale (CGAS) and Clinical Global Impression Scale (CGI) in psychiatry, these tools cannot be easily applied to children with autism spectrum disorder (ASD).

Objectives: The aim of this study is to examine the feasibility and inter-rater reliability of the Swedish versions of Developmental Disabilities

Children Global Assessment (DD-CGAS), a version of the CGAS modified for developmental disorders like ASD, and the OSU Autism Clinical Global Impression (OSU Autism CGI-S).

Methods: Sixteen clinicians (13 female, 3 male ) with varying professions and experience (> 2 yrs. and <2 yrs.) were recruited from 9 different child and adolescent psychiatry units in Stockholm County independently and spontaneously rate eight clinical vignettes of ASD for clinical referral and at discharge.

The vignettes consist of cases of ASD including clinical descriptions of everyday functioning and symptomatology. According to the clinical consensus ratings for the vignettes on the DD CGAS are 30-70, and 2-4 on the OSU Autism CGI Severity (S) Scale. The vignettes described cases of clinical heterogeneity with varying symptomatology and adaptive skills.

Statistical analyses, two-way random interclass correlation coefficients (ICC) in SPSS 20 were used to calculate interrater reliability for all vignettes and all possible pairs of raters for both the DD-CGAS and the OSU Autism CGI-S, as well as separately for experienced and less experienced clinicians. In addition to ICC, Pearson correlations between the DD CGAS and the OSU Autism CGI -S results were calculated.

Results: ICC for all raters (experienced and inexperienced) and points in time was .63 (95% CI= .34-.94) on the DD-CGAS and .60 (95% CI= .31-.93) on the OSU Autism CGI-S. On the DD-CGAS, ICC was 0.75 (95% CI = .45-.96, [ICC.78 referral-.79 discharge]) for experienced, and .58 (95% CI =.39-.96, [ICC.54 referral-.53 discharge]) for inexperienced clinicians. On the OSU Autism CGI-S, ICC was .72 (95% CI =.39-.96, [ICC.73 referral-.72 discharge]) for experienced and .59 (95% CI= .40-.79, [ICC.48 referral-.46 discharge]) for inexperienced clinicians. The correlation between DD CGAS and OSU CGI for referral was r= -0.86, SD=0.69 and the correlation between those instruments for discharge was r= -0.82, SD =0.28.

Conclusions: In a naturalistic clinical settings for agreement between experienced and inexperienced clinicians on the DD-CGAS and OSU Autism CGI-S is good to substantial. Correlation between DD-CGAS and OSU Autism CGI-S was high, both at referral and at discharge, which indicates a substantial association between severity of symptoms and functional impairment. DD-CGAS and OSU Autism CGI-S are promising, economic, intuitive tools to assess change for various clinical and research purposes in ASD.

**108.070 70** 3D Facial Pattern Analysis for Autism Using Geodesic Distances. T. Obafemi-Ajayi*[1], J. H. Miles[1], W. Qi[1], N. Takahashi[1], K. Aldridge[2], Y. Duan[1] and H. Ying[3], (1)*University of Missouri*, (2)*University of Missouri School of Medicine*, (3)*Nanyang Technological University*

Background:

The facial analysis is of great importance as it is related to brain development: "face mirrors brain". Recent studies suggest statistically significant differences in facial morphology for the various subgroups of children using 3D facial imaging data based on Euclidean distances. In this study, we apply 3D facial geodesic (surface) distance features as well as robust clustering analysis to identify etiologically discrete ASD subgroups.

Objectives:

To identify clinically meaningful clusters within ASD and the facial features that discriminate these clusters using 3D geodesic (surface) distance features. We seek to identify meaningful heterogeneity within the ASD dataset in comparison to the traditional autism subtypes (Autistic Disorder, Asperger Syndrome and PDD-NOS).

Methods:

We used the 3dMD software to obtain 3D coordinate data for a set of 19 anthropometric facial landmarks of our study sample of 62 ASD boys. All the boys were Caucasian between the ages of 8 and 12. To identify the potential subgroups, we applied different clustering techniques: Expectation Maximization, K-means, Partitioning around Medoids, and Self-Organizing Feature Map. We selected the optimal cluster configuration based on the cluster validation evaluation. The cluster results were validated clinically.

Results:

We identified 3 clusters with distinct geodesic facial features as well as meaningful clinical and

behavioral traits. The ASD subtypes (Autistic Disorder, Asperger Syndrome and PDD-NOS) were not evenly distributed within the 3 Clusters. Cluster 1 consists of mainly Autistic Disorder subjects (78.6%). Cluster 2 subjects consist of half Autistic Disorder (50%) and almost half Asperger Syndrome (44.4%) as well as one PDD boy. The Cluster 3 group is a mixed bouquet of diagnoses: (46.7% Autistic Disorder: 33.3% Asperger Syndrome: 20.0% PDD-NOS). PDD-NOS, the least precise autism diagnosis clinically, appears to be present most in the Cluster 3 group. The Cluster 1 group seemed to be the most compact and separate group facially, clinically and behaviorally. It consisted mainly of severe Autistic Disorder boys.

Conclusions:

There is a facial difference among autistic subjects. These facial differences show a spectrum of scale among the Autism diagnosis – Asperger Syndrome vs. Autistic Disorder. This implies that there are physical phenotypes related to Autism not just behavioral traits.

**108.071 71** A Review of Attention-Deficit/Hyperactivity Disorder Measures for Children with Autism Spectrum Disorder. S. A. Scott*, M. N. Gragg and S. A. Rutter, *University of Windsor*

Background: The new DSM-5 diagnostic criteria for Autism Spectrum Disorder (ASD) permit diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD) in individuals with ASD. Considerable phenotypic overlap exists between ASD and ADHD. It has been reported that approximately 30% of children with ADHD also meet the criteria for ASD, while approximately 50% of children with ASD meet the criteria for ADHD. Children with comorbid ASD and ADHD tend to experience more significant impairment in psychosocial, adaptive, and cognitive functioning; motor skills and executive control than children with a single diagnosis. Attentional difficulties, social impairment, and challenging behaviours are common in ADHD and ASD. Both disorders are more prevalent in boys than girls. However, social difficulties common in individuals with ADHD, such as peer rejection, are qualitatively different from the social disengagement and communication deficits present in individuals with ASD. Similar behaviours may have different antecedents; for example, tantrums may be due to intolerance to changes in routine in ASD, and to poor self-control or impulsivity in ADHD.

Objectives: It is essential that clinicians distinguish and identify commonalities between symptoms of ASD and ADHD. There is a need to delineate which ADHD measures are valid for ASD assessment. Thus, the purpose here was to review the literature on measures assessing ADHD symptoms in children with autism.

Methods: Peer-reviewed articles on ADHD assessment in children with ASD were retrieved using PsycInfo, PsycCritiques, PsycArticles, and PsycTests databases. Additional articles were identified from references in search-retrieved papers. Articles included in this review (a) utilized a sample of children with ASD; (b) used ADHD measures or interviews; and (c) reported psychometric properties of the instruments.

Results: Few measures have been specifically designed to assess comorbid ADHD in a population of children with ASD. The Hyperactivity and Attention Problems subscale scores from the Behavioral Assessment System for Children – Second Edition (BASC-2) have been used on both clinical and nonclinical samples of children with ASD. Normative data and clinical profiles for individuals (ages 2:0 through 21:11) with ASD are available for the BASC-2 parent and teacher report forms. Authors of the BASC-2 have reported high internal consistency, test-retest reliability, inter-rater reliability, and adequate concurrent validity. The Autism Spectrum Disorders – Comorbidity for Children (ASD-CC) is a measure of comorbid psychopathology for those with ASD. It is a 49-item rating scale assessing emotional difficulties, such as ADHD, which co-occur with ASD. The ASD-CC differentiates symptoms within the average range for children and adolescents with ASD from clinically significant symptoms. Developers of the ASD-CC have reported moderate inter-rater reliability, test-retest reliability, and validity. The Autism Comorbidity Interview – Present and Lifetime Version (ACI-PL) is a parent interview to identify comorbid psychopathology, such as ADHD, in ASD. The ACI-PL distinguishes between attention to special interests and general attention.

Conclusions: Clinicians need to address the phenotypic overlap between ASD and ADHD. A comprehensive assessment of ADHD when ASD is suspected is crucial, as treatment implications differ considerably between the two. Future

research should examine treatment methods for individuals with co-occurring ASD and ADHD.

**108.072 72** Abnormal Vestibulo-Ocular Reflexes and Possible Link to Cerebellar Deficits in Autism. T. B. Carson*, B. Wilkes, K. Patel, J. Welsh, M. H. Lewis and K. White, *University of Florida*

Background: Early identification and intervention have been shown to have a significant effect on the prognosis for children with autism spectrum disorders (ASD). It is also clear that the abnormal neurobiological processes resulting in ASD occur during fetal development and/or infancy long before the onset of the classic behavioral symptoms. Thus, identification of a bio-behavioral marker that occurs early in development and is related to the neurobiology of ASD would be particularly useful. Differences in sensory processing and motor coordination have been observed in children with ASD as early as 2 to 3 years of age. Motor control differences include decreased postural stability, decreased muscle tone, delayed motor milestones and altered vestibulo-ocular reflexes. Such motor deficits may share a common dependence upon appropriate processing of vestibular sensory input. The rotational vestibulo-ocular reflex (rVOR) functions to maintain stable vision by generating oculomotor responses to angular rotation head movements. The rVOR is useful for studying vestibular related sensory motor processing in this population as it involves a relatively simple reflex system, amenable to study in children with ASD.

Objectives: To determine whether vestibular sensory processing and related oculomotor control is compromised in ASD by testing rVOR function in ASD and typically developing (TD) children.

Methods: Fifteen children diagnosed with ASD and 16 TD children ages 6-12 participated in two types of whole body rVOR tests, performed on a computer controlled rotary chair: (1) velocity step tests (100º/second peak velocity) performed in 3 conditions (light, dark, and fixation suppression) and (2) sinusoidal harmonic acceleration tests (conducted at 0.05, 0.1 and 0.5 Hz frequencies with a peak velocity of 60º/second) performed in 2 conditions (dark and fixation suppression). For velocity step tests we assessed post rotary nystagmus gain, time constant of decay, and symmetry. For sinusoidal harmonic acceleration tests we assessed gain and phase lag.

Results: We observed three main differences in rVOR metrics including: (1) Participants with ASD exhibited greater time constant of decay of post-rotary nystagmus during velocity step tests in the dark and fixation suppression conditions, compared to TD controls; (2) Participants with ASD exhibited greater per-rotary nystagmus gain during velocity step tests in the dark condition, compared to TD controls;(3) Participants with ASD greater gain during sinusoidal harmonic acceleration (SHA) tests in the dark as well as fixation suppression conditions, compared to TD controls.

Conclusions: The current findings of greater gain and time constant of decay in participants with ASD indicate a lack of inhibition from the cerebellum to the brainstem velocity storage mechanisms in ASD. In particular, these findings indicate possible decreased Purkinje cell output to vestibular nuclei. Thus, rVOR may serve as a functional measure of pre- and post-natal neuropathological processes suspected in the cerebellum in ASD involving Purkinje cell loss and warrant further study. Furthermore, rVOR abnormalities could serve as a bio-behavioral marker if further study indicates they are reliably observed and specific to the ASD population.

**108.073 73** Adaptive Motor Impairment in Young Children with Autism Spectrum Disorders (ASD). I. Jalnapurkar*[1], E. O'Day[1], T. Paparella[2], S. Freeman[2] and S. S. Jeste[3], (1)*UCLA Center for Autism Research and Treatment*, (2)*University of California Los Angeles*, (3)*UCLA*

***Background:***

During infancy and early childhood, children use their motor skills to explore the environment, engage in physical play, initiate social interactions, and develop basic academic skills, thus playing a significant role in quality of life and social development. Motor delays and deficits have commonly been noted in children with Autism Spectrum Disorder (ASD), yet few studies have investigated adaptive motor function, or the performance of motor activities in daily life.

***Objectives*** :

The objectives of the study are to (1) characterize adaptive motor skills in young children with ASD using a standardized assessment, the Vineland Adaptive Behavior Scales-II (VABS-2) and to (2)

investigate the association of motor skills with core deficits, namely language and play.

***Methods:***

The data collected for this study are part of a larger study of preschoolers with ASD. The final sample included 100 participants with ASD between the ages of 23 and 82 months enrolled in the UCLA Early Childhood Partial Hospitalization Program (ECPHP) at the Resnick Neuropsychiatric Hospital. 30 age-matched, typically developing (TD) children from the greater Los Angeles area were recruited as controls. Adaptive motor function was evaluated by assessing gross and fine motor subscale scores of the ASD and TD groups with VABS-2. Other measures of interest, also collected as part of a clinical assessment prior to enrollment in the program, included the Mullen Scales of Early Learning, Wechsler Preschool and Primary Scale of Intelligence-IV, and the Developmental Play Assessment. Descriptive statistics were performed on adaptive motor function scores, and Pearson correlations were performed to investigate the association of adaptive gross and fine motor function with IQ, language, and play scores.

***Results:***

While there was a wide distribution in scores, children with ASD as a group demonstrated delays in adaptive gross motor (Mean=11.8; Range 6-18) and adaptive fine motor (Mean=12.0; Range=7-20) assessments of the VABS-2 (subdomain mean = 15; SD=2). Adaptive gross and fine motor function did not correlate with language ability but did correlate with non-verbal IQ and adaptive social function. Furthermore, higher scores on gross motor skills correlated significantly with lower level of functional play activity ($p$=0.041) with this inverse relationship stronger at higher play assessment levels ($p$=0.009).

***Conclusions:***

Although heterogeneity exists in motor ability, this study clearly indicates the presence of adaptive motor deficits in young children with ASD. It suggests the need to explore mediating factors, such as inattention or behavioral dysregulation in the relationship with core deficits, particularly in the inverse relationship with play levels. More comprehensive, prospective studies of adaptive motor function in young children, particularly in the context of targeted interventions may improve not only motor abilities but also core deficits within the autism spectrum.

**108.074 74** An Exploration of the Relationship Between the Child Behavior Checklist and ADOS Comparison Scores Including Possible Mediating Factors. L. A. Washington*[1], T. Katz[2], D. Sikora[3] and A. Shui[4], (1)*Rocky Mountain Human Services*, (2)*University of Colorado*, (3)*Providence Neurodevelopmental Center for Children*, (4)*Massachusettes General Hospital for Children*

Background: The Withdrawn syndrome scale and the Pervasive Developmental Problems (PDP) DSM-oriented scale on the Child Behavior Checklist (CBCL) have received attention in the literature as one way to identify children with symptoms consistent with an Autism Spectrum Disorder (ASD) diagnosis. Although previous research has supported a relationship between the CBCL Withdrawn scale and an ASD diagnosis, inconsistent results have emerged regarding the relationship between the PDP scale and an ASD diagnosis. However, Gotham et al.'s work (2009) in developing calibrated ADOS Comparison Scores now allows for an examination of these scores as they relate to both the Withdrawn and PDP scales. ADOS Comparison Scores range from 1-10 and are divided into four interpretive categories that correspond to the level of autism spectrum-related symptomatology that is observed during the ADOS or ADOS-2.

Objectives: The aim of the present analysis was to further explore the relationship between the Withdrawn and PDP CBCL scales and ADOS Comparison Scores while taking into account possible confounding effects of child race or ethnicity, sex, and cognitive ability.

Methods: Data were obtained from 2161 children between the ages of 2 and 5 years who participated in the Autism Treatment Network. Subjects were included if they had a calculated ADOS Comparison Score, a complete parent-report CBCL, and had completed a standardized measure of cognitive or developmental ability (overall IQ).

Results: Correlational analyses indicated a significant relationship ($p<.01$) between ADOS Comparison Scores and T-scores of multiple CBCL scales, including the Withdrawn scale ($p<.0001$).

The relationship between ADOS Comparison Scores and the PDP Scales approached significance at the .01 level (p=.0190). However, when T-scores on both the Withdrawn and PDP scales were greater than 65, the relationship between Comparison Scores and PDP T-scores was no longer significant. Gender, race, and ethnicity did not change the relationship between Withdrawn and PDP T-scores and Comparison Scores. After controlling for overall IQ, the relationship between Comparison Scores and PDP T-scores was no longer significant while the relationship between Comparison Scores and Withdrawn T-scores remained significant.

Conclusions: Although CBCL Withdrawn and PDP scale T-scores were significantly correlated with ADOS Comparison Scores in the present study, the relationship was complicated by the impact of overall IQ. It is possible that the items unique to the PDP scale capture behaviors of children with lower cognitive abilities and artificially inflate the relationship between this scale and ADOS Comparison Scores. Our results suggest that caution should be exercised when CBCL PDP scale scores are used to indicate the presence of ASD as designated by higher ADOS Comparison Scores as a greater number of false positives are likely unless cognitive level is accounted for.

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**108.075 75** Assessment of Cognitive and Language Abilities in Toddlers with and without Autism Spectrum Disorders: Comparison of the Mullen Scales of Early Learning and the Bayley Scales of Infant and Toddler Development, 3rd Edition. M. D. Lense*, S. Hoffenberg, E. S. Mitchell, C. Hall and C. Klaiman, *Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*

Background: Valid and reliable assessment of cognitive and language development in young children is a key component of diagnostic evaluations for autism spectrum disorders (ASD), developmental delay, and language disorders. The Mullen Scales of Early Learning and Bayley Scales of Infant and Toddler Development, 3rd edition are the most commonly used standardized measures to assess early cognitive development because they are normed from infancy through the preschool years. While the Bayley Scales are frequently used in clinical settings, the Mullen Scales are more widely used in research studies, particularly with children with or at risk for ASD. A study presented at IMFAR 2008 (Esler et al, 2008) found strong correlations between the measures for nonverbal mental age but standard scores were not correlated. These findings need to be replicated in a more heterogeneous sample in order to better understand the implications of translating research findings to the community. In addition, Esler and colleagues (2008) only looked at the nonverbal domains; as such it is important to also understand the comparability of the language domains.

Objectives: Examine convergent validity of the nonverbal cognitive, receptive language, and expressive language subscales on the Mullen and Bayley Scales in toddlers with and without ASD.

Methods: The Mullen and Bayley scales were administered to participants from 12-42 months of age who were seen for a research or clinical assessment due to a diagnostic question of ASD, as well as typically developing (TD) controls. Data has been collected on 11 individuals to date, with expectations of 50 participants by April 2014. ASD diagnosis was determined through a full evaluation including cognitive and diagnostic measures (i.e., Autism Diagnostic Observation Schedule (ADOS)), as well as behavioral observations and parent interviews.

Results: Toddlers with ASD had lower standard scores on both the Mullen and Bayley scales than TD controls. Preliminary results across the sample indicate strong correlations for standard scores and age equivalence scores for the Mullen and Bayley nonverbal cognitive, receptive language, and expressive language subscales (r's>0.8, p's<=0.001). However, for some TD and ASD participants, scores on any particular subscale differed by more than one standard deviation, though performance was not consistently greater for one test versus the other.

Conclusions: Preliminary findings suggest, unlike the Esler et al (2009) findings, good concordance between the Mullen and Bayley nonverbal

cognitive, receptive language, and expressive language scales when examining a sample that includes toddlers both with and without ASD. Indeed, correlations between the Mullen and Bayley scales were similar to the test-retest correlations for each of the individual measures. Differences in participants' level of functioning between the current and Esler studies may explain this variability. Analyses based on specific diagnostic group are ongoing. Research studies often examine cognitive or language performance on the Mullen as a predictor or covariate in paradigms of behavior or brain function in ASD versus TD individuals. Results suggest that these findings in research settings may translate to toddlers seen through community practices that rely on the Bayley scales.

**108.076 76** Autism Symptomatology Associated with Developmental and Adaptive Behavior in Infants with Fragile X Syndrome and Autism Infant Siblings. K. E. Caravella*, L. M. McCary and J. E. Roberts, *University of South Carolina*

Background: Fragile X syndrome (FXS) is the number one single-gene cause of autism spectrum disorder (ASD) with approximately 35% of males with FXS meeting criteria for autism. Previous research has examined relationships between ASD symptomatology and both adaptive behavior and cognitive functioning in idiopathic ASD. Findings suggest significant, but small, negative correlations between both adaptive communication and socialization skills, and verbal and performance IQ with ASD symptomatology (as measured by the ADOS) in adolescents (Klin et al., 2007) and between adaptive communication and daily living skills and ASD symptomatology in toddlers (Ray-Subramanian et al., 2011). Correlations between developmental measures and ADOS scores were not reported in the toddler sample. To our knowledge, no published study has examined the relationship of adaptive behavior and developmental skills to autism symptomology in infants at risk for ASD.

Objectives: Preliminary data from an ongoing study expands this literature by examining the relationships between autism symptomatology and both cognitive and adaptive functioning in infants at risk for ASD (FXS and autism infant siblings) utilizing the Autism Observation Scale for Infants (AOSI, Bryson et al., 2008), a standardized measure of autism features in infants.

Methods: Participants included 20 male infants at 12 months of age who are part of a longitudinal study examining early development in infants at risk for ASD. Infant siblings of a child with autism (ASIB, n=11) and infants with FXS (n=9) participated. Measures of autism symptoms (AOSI), developmental skills (Mullen Scales of Early Learning), and adaptive functioning (Vineland Adaptive Behavior Scales II – Survey Interview Form) were obtained. Pearson product moment correlations were run to examine the relationship between AOSI total scores and domain standard scores on the Vineland and age equivalent scores on the Mullen. Age equivalents were used on the Mullen to combat floor effects evident in the standard scores that were not observed in the Vineland.

Results: Correlations reveal a moderate negative relationship between the AOSI and the Expressive Language ($r$ =-.60; $r$ = -.52) and Fine Motor ($r$ =-.62; $r$ = -.59) domains of the Mullen for the ASIBs and FXS infants respectively. These results suggest that increased autism symptoms were associated with decreased expressive language and lower fine motor skills in both groups at high risk for autism. There was no relationship between the AOSI and other domains of the Mullen and Vineland for either group.

Conclusions: These findings are congruent with findings in older-aged samples, that higher autism symptomatology is related to lower verbal and motor functioning (Landa et al., 2013). Understanding early developmental profiles in children at heightened risk for ASD is critical to facilitate early diagnosis and guide targeted treatment to help ameliorate symptoms in key developmental periods. This study is the first to examine relationships between ASD symptomotology and both adaptive behavior and developmental skills in infants at risk for ASD. We anticipate data from at least 8 additional participants (4 in each group) by conference presentation time.

**108.077 77** Behavior Economic Measures of Social Reward in Children with Autism. N. Call*[1], J. E. Lomas Mevers[2] and A. R. Reavis[1], (1)*Marcus Autism Center & Children's Healthcare of Atlanta*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University*

Background:

There is an emerging supposition that the social impairments that are part of the autism phenotype originate from a failure to experience social interactions as rewarding (Dawson et al., 1998; Dawson, Carver, Meltzoff, Panagiotides, & MacPartland, 2002; Dawson, Webb, & McPartland, 2005; Mundy, 1995; Rochat & Striano; Schultz, 2005). As such, there is a need for objective measures of social reward. Such a task is ideally suited to the subfield of psychology known as behavioral economics, the methods of which emphasize precise and direct quantification of reward value. Within this discipline, reward value is commonly measured based upon how hard an individual will work for a particular outcome. In the case of social reward, children with ASD would be expected to work less at a task for the opportunity to engage in social interactions than would typically developing (TD) children. Progressive ratio (PR) methodologies examine an individual's consumption of a reward at various "prices", which are represented by the number of times they must perform a task for the reward. Data from PR procedures are examined in terms of consumption at several key points along the price continuum. For example, the *break point* is the most an individual will work for a reward. $O_{max}$ is the point along the price/responding function at which working begins to decelerate as a result of increases in price.

Objectives:

The present study employed a PR arrangement to compare the degree to which children with autism and TD peers valued social attention.

Methods:

Fourteen children, ages 3 - 8 participated, 5 with an ASD diagnosis and 9 TD individuals. Each participant completed a PR procedure that involved working at a task (i.e., pressing a microswitch). The procedures compared each participant's performance on a PR arrangement for two different types of rewards: 30 s of attention from a novel adult, or access to a highly preferred item. The number of tasks that had to be completed increased within each series until one minute elapsed without any task completion.

Results:

Four out of five participants with autism showed higher breakpoints and Omax values for preferred items than for the social attention. On average, participants in the ASD group emitted 732% more responding towards preferred item than attention. This pattern was reversed in the TD group, with seven of nine showing higher breakpoints and Omax values for attention than preferred items. On average, participants in the TD group emitted 460% more responding for attention than for preferred items.

Conclusions:

Behavioral economic measures of social reward effectively quantified the degree to which individuals with autism value social reward. This method effectively differentiated between individuals from ASD and TD groups, and offers a level of precision in quantification of social reward that is much greater than in existing measures.

**108.078 78** Comparison of Parent and Teacher Reports of Adaptive Functioning for Children and Adolescents with Autism Spectrum Disorders. J. Ginberg*[1], J. Pandey[2], R. T. Schultz[1] and S. Paterson[2], (1)*University of Pennsylvania*, (2)*The Children's Hospital of Philadelphia*

Background:

The Vineland-II, a leading measure for studying adaptive functioning, contains different forms for teachers and parents, but there have been few studies comparing informant effects. Children and adolescents with autism spectrum disorders (ASD) have significant deficits in their adaptive skills, which include the age-appropriate behaviors that are needed to live and function independently in the real world. While IQ has been found to be a strong predictor of adaptive behavior in low functioning individuals with ASD, this gap is increased for higher functioning individuals. This suggests the importance of understanding how IQ interacts with and contributes to adaptive functioning.

Objectives:

The aim of this study is to compare parent and teacher reports on the Vineland-II for children and adolescents with ASD. The relationship of those reports will be examined while controlling separately for cognitive functioning, symptom severity, SRS total score, and SCQ. In addition,

the contribution of IQ to the score of adaptive functioning will be examined.

Methods:

Participants include 200 individuals with ASD (183 males, 17 females) between 6 and 18 years of age (mean age=12.02 years, SD 3.12 years). Chi-square analyses and Pearson correlations were run between Vineland-II scores for parent and teacher reports in the Communication, Daily Living Skills, and Socialization domains and each of their subscales. Partial correlations were also run, controlling for cognitive functioning, ADOS severity score, SRS total score, and SCQ scores separately.

Results:

Teachers rated participants higher than parents did for all three domains analyzed in this study. There was a significant difference between parent and teacher mean scores for the Communication and Daily Living Skills domain, but not for Socialization. Significant correlations were found between parent and teacher reports for all of the domains. However, after controlling for IQ, these were no longer significant. SRS total score, SCQ, and ADOS severity score had no significant effect on correlations.

Conclusions:

Children and adolescents with ASD have difficulty applying their cognitive abilities to everyday skills. Teachers and parents interact with individuals with ASD in different settings for varying lengths of time and may have different expectations and thresholds for their appraisal of children's skills. In addition, informants may differ on how they interpret their view of an individual with higher or lower IQ. Therefore, it is important to consider the viewpoints of multiple informants to obtain a more comprehensive evaluation of an individual with ASD that can be useful in the creation of appropriate and efficient diagnosis and planning.

**108.079 79** Comparisons Between Black and White Children Included in the Autism Treatment Network Registry. A. D. Hagen*[1], A. P. Hill[2], K. E. Zuckerman[2] and E. Fombonne[2], (1)*OHSU*, (2)*Oregon Health & Science University*

Background: Prevalence rates of ASD are lower in Black children (1%) compared to White children (1.2%). Black children are diagnosed at an older age. Whether or not underdetection is paralleled by differing clinical presentation is not known.

Objectives: To evaluate differences between Black and White children in a large clinical sample of children referred for and diagnosed with ASD.

Methods: Data collected in 18 ATN sites from 2007 to 2013 were obtained. We included in this analysis 244 Black subjects who were matched by gender, age and clinical site to 488 White children. They ranged in age from 1.5 to 15.9 years with no difference between Black and White children. There were 82.8% boys and 17.2% girls.

Results:

There was no difference between Black and White children for their repartition by ATN site. Children from Black families had significantly lower parental education (chi-2=25.1, 5 df; p<.001). When assessed with the ADOS, both groups showed similar overall levels of autistic symptoms, as assessed by Calibrated Severity scores from the ADOS, that showed no difference for Social Affect, Restricted Repetitive Behavior, and Total scores (all comparisons: NS). However, item score analyses showed better Eye Contact in BIack children, fewer Vocalizations, more Stereotyped Utterances, and less Sharing. In younger children assessed with the Mullen Scales of Early Learning, Black children had significantly lower scores on the Early Learning Composite (52.1 vs 54.6; p=.03). Older children who had a Stanford-Binet abbreviated IQ score, showed similar differences, with Black children scoring lower than White children (61.7 vs 66.7; p=.08). Similarly, Black children with full Stanford-Binet assessments showed consistent trends (p>.05 and <.15) for having lower scores than White children with a 6- to 7-point difference on standardized scores. On CBCL scores, Black children showed significantly higher scores on the Anxiety Problems narrow-band scale (57.0 vs 55.2; p=.01), lower scores for Somatic Complaints (57.3 vs 58.9; p=.02), and no difference for Withdrawal, Attention Problems, Aggressive Behaviors, Internalizing, Externalizing and Total CBCL scores. With the exception of the Communication score that showed lower proficiency in Black children as compared to White children (61.9 vs 65.3; p<.01), all other Vineland Adaptive Behaviors scores showed no differences. Antihistaminic drugs were prescribed more

frequently in Black children (10.2% vs 4.9%; Fisher exact test: p=0.011); otherwise, no difference was found for prescribed drugs, including amphetamine derivatives, atomoxetine, alpha-2 adrenergic antagonists, anticonvulsants, SSRI's, and atypical neuroleptics.

Conclusions: Greater communication and cognitive delay, as well as anxiety symptoms, seem more prevalent in Black than White children in this referred sample. The limitations of a study relying on referred children only will be discussed.

**108.080 80** Confirmatory Factor Analysis of the Social Responsiveness Scale. K. LaGuerre*[1], F. I. Jackson[1], E. Hanson[1] and A. V. Snow[2], (1)*Boston Children's Hospital*, (2)*Boston Children's Hospital, Harvard Medical School*

Background: The Social Responsiveness Scale (SRS; Constantino et al, 2003) is a questionnaire that measures social impairment and symptoms of autism spectrum disorders (ASD). Several studies have examined the psychometric properties of the SRS and have reported positive results (e.g., Constantino et al, 2007; Constantino & Gruber, 2005; Constantino et al, 2004; Pine et al, 2006). Examinations of the construct validity of the SRS have included several studies that have used principal components analysis to determine the underlying structure of the measure (e.g., Bolte et al., 2008; Constantino et al., 2000). Constantino et al. (2000) reported that a single factor solution best described the data. These results were corroborated in a study by Bolte et al (2008) who reported a single factor solution of ASD symptomology in both normative and clinical samples. However, other investigators have suggested that the SRS may measure overall behavioral impairment rather that ASD-related symptomology (Hus et al., 2013).

Objectives: The purpose of the current study was to assess the construct validity of the SRS by testing the single factor model of the measure in a large, representative sample of children with ASD. To our knowledge, this is the first independent study of the factor structure of the SRS.

Methods: Participants in this study included 395 individuals (82% males) between the ages of 29 and 272 months (mean=102.5, SD=48.77) who participated in the Simons Simplex Collection and Autism Consortium at Boston Children's Hospital. All individuals were diagnosed with an ASD. CFA was used to test a single factor model of the SRS. Model fit was estimated using the Tucker Lewis Index (TLI), Comparative Fit Index (CFI), and Root Mean Square Error of Approximation (RMSEA). As suggested by Hua and Bentlerb (1999), the following cutoffs were used for good fit: >.90, >.90 and <.06, respectively.

Results: The CFA indicated an RMSEA of .068, which is slightly higher than the cutoff suggested by Hua et al. The CFI was .58, and the TLI was .57. Both indices were lower than the proposed cutoff of >.90 to suggest good fit. Factor loadings for the one-factor solution ranged from .06 to .71. When a factor loading cutoff of .3 was used, 10 items (15% of the total items) did not load onto the one factor solution.

Conclusions: Our results indicate that a one-factor solution may not be optimal to describe the structure of the SRS. All fit indices were below proposed cutoffs for good fit, and 15% of the SRS items did not load onto a one factor model. These preliminary results suggest that further investigation of the construct validity of the SRS is necessary. Future analyses will include CFA of 2- and 3-factor solutions. We will test a 2 factor solution of social/communication and restricted and repetitive behaviors, and a 3 factor solution of social, communication, and restricted and repetitive behaviors, which replicate ASD symptomology as classified by the DSM-5 and DSM-IV, respectively.

**108.081 81** DATA Mining of Clinical Variables and Biological Endophenotypes in Autistic Patients Using Fourth Generation Artificial Neural Networks. R. Sacco*[1], S. Gabriele[2], E. Grossi[3], P. M. Buscema[4] and A. M. Persico[2], (1)*IRCCS Fondazione Santa Lucia*, (2)*Univ. Campus Bio-Medico*, (3)*Villa Santa Maria Institute*, (4)*Semeion Research Center*

Background: Several studies have attempted to partition autistic individuals into subtypes ideally homogeneous in terms of clinical presentation and/or underlying pathogenesis. Clinical subtyping has been defined one of the major short-term challenges in child and adolescent psychiatry. This is especially true for autism research, since clinical heterogeneity represents one of the hallmarks of ASD. We have recently analyzed the autistic phenotype taking into account observable behaviors, patient- and family-history variables, and biological endophenotypes. Using principal component and cluster analysis on 245 patients, we previously described at least four principal

components and four patient clusters (Sacco et al., Autism Res. 2010 and 2012).

Objectives: To identify specific patterns linking biological endophenotypes, such as macrocephaly and elevated serotonin blood levels, to autism clinical profiles.

Methods: Artificial Neural Network were applied to a complete data set of 110 ASD patients encompassing 25 variables spanning clinical features, family history, morphological and biochemical quantitative traits. We applied semantic connectivity maps (AutoCM), a fourth generation artificial neural network able to detect non-linear trends and associations among variables with significantly greater power as compared to the traditional parametric statistics employed in our previous study. The matrix of connections, visualized through the minimum spanning tree, maintains non-linear associations among variables and captures schemes among clusters of variables. The strength of association in semantic connectivity maps ranges from 0 to 1 (i.e., from no to full association).

Results: [1] clinical variables tend to cluster around two configurations: (a) "lower functioning", which has its central node in the presence of motor stereotypies, strongly connected with intellectual disability (0.99), verbal stereotypies (0.98), hyperactivity (0.98), reduced pain sensitivity (0.97), history of regression (0.94) and self-injurious behaviors (0.93); (b) "higher functioning", which has its two central nodes in positive history of allergies or immune disease in the patient, or in first-degree relatives, tightly linked to each other (0.97) and with obstetric complications (0.97), delayed onset of social smile (0.97), presence of any infectious disease at autism onset (0.96), pre-term delivery (0.89), normal intellectual level (0.89), and a DSM-IV Asperger (0.88) or PDD-NOS (0.85) diagnosis. [2] Macrocephaly is associated with a positive history of allergy and immune disease in first-degree relatives (0.92) and to a lesser extent with muscle hypotonia (0.77). [3] Hyperserotoninemia may be connected with abnormal EEG pattern and/or history of seizures in males (0.80), whereas in females it appears linked to positive history of allergy/immune disease in first-degree relatives and muscle hypotonia, although sample size limitations for females do not yet allow reliable coefficient estimations.

Conclusions:

AutoCM algorithms show several complex patterns which replicate and largely extend previous findings obtained with parametric approaches. New insights, such as those possibly linking hyperserotoninemia with abnormal EEG patterns, if replicated may allow novel hypothesis generation and experimental designs. These results will be replicated in an independent sample, so as to better define the relationship between biological endophenotypes, biomarkers and clinical features involved in autism.

**108.082 82** Development and Pilot of the Caregiver Strategies Inventory: Measuring Parents' Everyday Responses to Children's Sensory Features. A. V. Kirby*, W. Zhang and G. T. Baranek, *University of North Carolina at Chapel Hill*

Background: Sensory features (i.e., hyperresponsiveness, hyporesponsiveness, sensory seeking, and enhanced perception) are prevalent in 40-90% of individuals with autism spectrum disorder (ASD) (Baranek et al., in press). These features were recently added to the diagnostic classification of ASD in the DSM-5 (APA, 2013) and are understood to impact participation in everyday activities for children with ASD and their families (Bagby et al., 2012). Research suggests caregivers use many different strategies in attempt to manage their children's sensory features in the course of their daily routines (Schaaf et al., 2011). However, the frequency with which they use particular strategies may differentially impact child outcomes in previously unexplored ways.

Objectives: To design and pilot a questionnaire to quantify caregiver responses to sensory features within three conceptually-distinct categories: cognitive-behavioral strategies, sensory-perceptual strategies, and avoidance strategies.

Methods: Designed as a companion tool to the Sensory Experiences Questionnaire (SEQ; Baranek, 2009), the Caregiver Strategies Inventory (CSI) measures strategies parents of children with ASD use to manage their children's sensory features in everyday activities. On the CSI, caregivers rate the frequency (6-point scale, 0='not at all' to 5='every time') with which they implement each of five different strategy types (2

sensory-perceptual, 2 cognitive-behavioral, and 1 avoidance) during 22 different sensory situations. Situations were chosen based on SEQ items with factor loadings ≥0.4 from a confirmatory factor model (Ausderau et al., in press) and/or ≥70% parent strategy endorsement (Little et al., 2011). Strategy options were based on conceptually-grouped caregiver responses to open-ended questions collected over a decade (*N*=1056). Three researchers expert in ASD, cognitive-behavioral theories, and/or sensory features reviewed the questionnaire and subsequent adjustments were made. The CSI was piloted as an online survey through Qualtrics with a national sample of 187 families of children with ASD (ages 4-14 years) to determine internal consistency, explore preliminary associations, and collect parent feedback.

Results: Internal consistency values for conceptual strategies were strong: cognitive-behavioral, α= .95; sensory-perceptual, α=.95; avoidance, α= .85. Overall, parents reported cognitive-behavioral strategy use most often (*M*=2.24, *SD*=0.71), followed by sensory-perceptual (*M*=1.91, *SD*=0.71), and avoidance strategies (*M*=1.22, *SD*=0.61). Preliminary regression analyses (significant at $p<0.05$) suggest that sensory-perceptual strategy use was partially driven by younger chronological age and lower intellectual functioning, cognitive-behavioral strategy use by younger chronological age, and avoidance strategy use by lower intellectual functioning. The overwhelming majority of participants agreed that scenarios were easy to understand (96%) and relevant to their child (87%), that strategies were easy to understand (100%) and reflected strategies they use (88%), and that they would be willing to take this questionnaire again in future studies (100%).

Conclusions: Based on pilot data, the CSI has utility for measuring caregiver strategies and, importantly, received positive feedback from parents. Preliminary analyses suggest parents' strategy choices may differ as a function of chronological age and intellectual functioning. The CSI can be used in future work to explore differential impacts of caregiver strategies on child outcomes longitudinally. This knowledge will ultimately inform parent training on best practices for addressing sensory features during everyday activities.

**108.083 83** Discriminative Validity of Social Responsiveness Scale (SRS) on Autism Diagnoses from a Community Study in Taiwan.

W. T. Kao*[1], R. A. Harrington[2], C. H. Tsai[3], I. T. Li[4], P. C. Tsai[5], C. L. Chang[6], C. C. Chien[7], C. C. Wu[8], C. L. Chu[9], H. Y. Hsu[4], F. W. Lung[10] and L. C. Lee[5], (1)*National Defense Medical Center*, (2)*Johns Hopkins University*, (3)*Kaohsiung Municipal Kai-Syuan Psychiatric Hospital*, (4)*Kaohsiung Medical University Chung-Ho Memorial Hospital*, (5)*Johns Hopkins Bloomberg School of Public Health*, (6)*Graduate Institue of Medicine, Kaohsiung Medical University*, (7)*Kaohsiung Armed Forces General Hospital*, (8)*Department of Psychology, Kaohsiung Medical University*, (9)*National Chung Cheng University*, (10)*Taipei City Hospital*

Background: Researchers generally agree that autism spectrum disorder (ASD) represents one end of a spectrum of quantitative impairment that is continuously distributed in the general population. The Social Responsiveness Scale (SRS) is a 65-item scale that characterizes quantitative impairments in social communication and repetitive behavior/restricted interests that define ASD, and therefore are expected to distinguish ASD from other developmental disabilities (DD) and development that is not affected by ASD or other DD. We previously reported that SRS total and subscale scores distinguished significantly between ASD and other developmental disorders from a clinic-based study in Taiwan (Wang 2012); however, it is unknown similar findings can be replicated with a community-based study design.

Objectives: This study aimed to examine the discriminative validity of individual items and different cut-offs of the SRS, on ADOS, and clinician-determined ASD diagnoses.

Methods: A community-based study of autism in school children aged 6-8 was conducted in Taiwan. Study participants were first screened using the SCQ and SRS. Children with parent-reported SCQ scores>=7 were invited for a clinical visit. Twenty-seven boys and nineteen girls, and their primary caregiver, participated in the clinical visit which comprised the Autism Diagnostic Observation Schedule (ADOS), the Autism Diagnostic Interview-Revised (ADI-R), and a comprehensive evaluation with a child psychiatrist. Three groups were classified based on the ADOS: ASD (n=12), subclinical (n=8), and unaffected (n=25). The 3 groups based on clinical judgment were: ASD (n=7), other DD (n=24), and unaffected with ASD or other DD (n=15). Two

cut-offs for the SRS were used to define higher versus lower risk for ASD. As recommended in the SRS manual, a raw score of >=70 in males and >=65 in females is a cut-point that provides evidence for the presence of an ASD. A raw score >=85 is considered "very strong evidence" of the presence of an ASD as suggested by studies from Western countries.

Results: Only 3, out of 65, items on the SRS statistically significant discriminate the 3 ADOS determined diagnostic groups; similarly, only 4 items statistically significant discriminate the child psychiatrist's diagnostic groups. The cut-off of >=85, but not the high risk cut-off (>=70 in males and >=65 in females), significantly discriminate diagnostic groups that were determined by the child psychiatrists (p=0.02). However, neither of the cut-offs discriminate ADOS determined groups.

Conclusions: Our results do not concur with findings from our clinic-based study, where we reported the SRS successfully distinguished Taiwanese children with ASDs from typical controls as well as from individuals with other psychiatric diagnoses. Possible reasons for the discrepant findings include: 1) This community-based study, with a multi-stage case identification design, yields smaller numbers of cases than our prior study, 2) Individual items on the SRS rather than the SRS full scale and domain scores were used to test the discriminative validity in this current study, and 3) Reported behavioral symptoms on participants recruited from a clinic setting may be different from those from the community. Our findings hint sub-domains of the SRS with different cut-offs may be needed for community-based studies.

**108.084 84** Do Kindergarten-Level Behaviour Profiles of Children with Autism Spectrum Disorder (ASD) Differ from Profiles of Children with Other Developmental Disabilities?. E. Duku*[1], M. Janus[1], E. Mauti[1], M. Horner[1] and P. Szatmari[2], (1)*McMaster University*, (2)*University of Toronto*

**Background:** The possible increases in the prevalence of Autism Spectrum Disorder (ASD), the burden it causes, and the inconsistencies in timing and accuracy of ASD diagnoses together suggest a need for system-level changes in the way the needs of children with ASD are addressed. Tools facilitating allocation of intervention strategies for children at early ages, who may not even have a confirmed ASD diagnosis yet have potential to alleviate the burden of this disorder. In Ontario, Canada, developmental data are collected for all kindergarten children at regular intervals with the Early Development Instrument (EDI). For a proportion of three cohorts, it was possible to ascertain whether these children were diagnosed with ASD or any other developmental disability by age 9. This sample is investigated here for potential kindergarten behaviour patterns that may distinguish children with ASD from those with other disorders.

**Objectives:** To establish whether kindergarten age behaviour profiles of children with ASD differ from those of children with other developmental disabilities, and from those of typically developing children.

**Methods:** The EDI is a teacher-completed questionnaire measuring developmental health across five domains: Physical Health and Well-Being, Social Competence, Emotional Maturity, Language and Cognitive Development, and Communication Skills and General Knowledge. The EDI included information on whether or not a child had identified special needs (SN) in kindergarten.

The analyses were based on EDI data collected from 2005-2007 matched at child level with Grade 3 provincial test data collected from 2008-2010. Approximately 57% of the available data were matched, creating a sample of 63,870 children (50.6% boys, mean age 5.7 years). The provincial databases provided information on whether a child had ASD or another developmental delay in Grade 3. MANOVAs compared EDI scores on domains and subdomains between children with and without a grade 3 ASD diagnosis. Children with an ASD or other delay in Grade 3 who also had SN in kindergarten were considered as "early identified", while those without SN as "late identified".

**Results:** Children with Grade 3-ASD and with Grade 3-other delay scored lower than typically developing children on all domains. Children who were "early identified" had consistently lower scores than those "late identified". In both groups, however, children with ASD had lower scores in the Social Competence and Emotional Maturity domains than children with other delays, but better in the Language and Cognitive Development domain. Among the "early

identified", children with ASD also had better scores in Physical Health and Well-being than children with other delays.

**Conclusions:** Our analyses indicate that children with ASD can be distinguished on broad characteristics of their behavioural profile from children with other disabilities; they function better in cognitive areas but worse in social-emotional areas. Further research is needed to examine more specific areas within the broad domains to increase the description's precision. Our results indicate that the population-based collection of EDI data can assist in monitoring the prevalence of children with ASD-like characteristics and thus could help in making decisions about allocating necessary resources within the educational system and beyond.

**108.085 85** Evaluating Student Social Behavior: An Initial Comparison of Systematic Direct Observation and Direct Teacher Behavior Ratings. S. A. Owens*[1], S. Kilgus[2], A. M. Schoemann[2], T. C. Riley-Tillman[1] and J. P. Stichter[1], (1)*University of Missouri*, (2)*East Carolina University*

Background: Currently in the field of special education, federal mandates (IDEA, NCLB) not only promote, but also require, the implementation of evidence based practices (EBPs) for students with disabilities (Cook & Cook, 2011). In response to closing research to practice gaps, organizations such as What Works Clearinghouse seek to identify potential EBPs for specific populations. One specific area of education for which the need for clarity regarding appropriate EBPs has been increasingly felt, is for students with autism. As professionals seek to identify and implement strong manualized interventions targeting this population, it becomes increasingly necessary to effectively monitor student's progress, providing implications for tailored dosage to meet individualized needs. Systematic direct observation (SDO) is a common method for ongoing assessment used to monitor behavior and associated intervention effects. While SDOs are generally considered the most appropriate and accepted means of measuring student behavior, SDO produces a number of limitations such as Hawthorn effects and are time intensive. A related measure, Direct Behavior Rating (DBR) is a scale that provides a direct rating of behavior(s) immediately following the observation of a student in regard to domains identified as significant moderators of student success. This measure is meant to be brief and immediate in nature, allowing for repeated use over time and implications to inform practice, similar to SDO. As EBP implementation increases, means of effectively and efficiently monitoring progress and informing practice in a feasible manner is vital.

Objectives: The Social Competence Intervention for Adolescents (SCI-A) is a targeted EBP designed to meet the specific social needs (Stichter, et al., 2010) of youth with ASD or similar challenges. The current study seeks to examine the reliability of SDO and DBR as a potential efficient assessment of progress in relevant domains of student functioning in response to SCI-A intervention effects.

Methods: This project will examine the agreement across five target behaviors through 15-minute systematic direct observations at 3 time points. Concurrently, classroom teachers rated the same target students (DBR). Student behaviors included active engagement, disruptiveness, respect, and appropriate social interactions with peers and teachers. This examination occurred for thirty- three students middle students as part of a larger RCT investigation of the efficacy of the (SCI) program.

Results: A review of overall correlations indicated a strong relationship between SDO and DBR for active engagement (AE), but smaller correlations for remaining pairings. DBR and OCF data were then disaggregated and compared within time point. Results indicated that the relationships between DBR and OCF scales were moderate to strong at baseline. Yet, correlations attenuated over time within each DBR-OCF pairing. This was with the exception of AE, which remained strong across all time points.

Conclusions:

A brief, immediate measure that informs practice is as essential as EBPs for students with ASD. Without an effective manner to progress monitor, the research to practice gap can't close. The current N draws caution, nevertheless, suggests the DBR compares well to the SDO. Furthermore, teachers may be less responsive to ongoing social change.

**108.086 86** Executive Dysfunction Is More Predictive of Adaptive Functioning in a Sample of High-Functioning Autism. L. D.

Ankeny* and S. L. Hepburn, *JFK Partners/University of Colorado School of Medicine*

Background: Individuals with ASD display a varied profile of executive functioning across domains, although these deficits do not appear to be universal. While individuals with high-functioning ASD (HFA; IQ >70) often exhibit adequate performance on behavioral tasks of executive functioning when compared to controls, parent and caregivers often report significant difficulties with behavior regulation in real-life. The discrepancy between performance on behavioral tasks and ratings of real-world behavior is striking and necessitates further investigation to elucidate these differences.

Objectives: To examine the relationship between parent-report of executive function abilities and adaptive behaviors in a cohort of individuals diagnosed with autism, with and without intellectual disability (ID), as well as an ID sample without ASD.

Methods: A cohort of 37 individuals was drawn from a larger sample of an ongoing, longitudinal study. A wealth of diagnostic, phenotypic and descriptive data is available both for this current time point (T3), as well as from earlier assessments. The focus of the current study is drawing from parent report measures of executive function (BRIEF) and adaptive functioning (Vineland). Additional measures may be included as predictive variables if warranted.

Results: Comparison of ASD (IQ >70) to DD (IQ < 70) shows a significant group difference on the BRIEF Metacognition Composite ($p = .020$); Global Executive Composite ($p = .021$) and a trend for Behavior Regulation Index ($p = .058$). Interestingly, the group differences were not in the hypothesized direction, finding that individuals with ASD performed worse on ratings of executive measures than those in the DD group. There were no significant group differences in overall adaptive behavior (Vineland Adaptive Behavior Composite, $p = .297$)

Conclusions: These data indicate that measures of executive function may be more predictive of adaptive functioning than IQ in a high-functioning ASD sample. Additionally, the lack of a group difference on overall adaptive functioning necessitates further understanding of what factors (e.g. IQ vs. impaired EF) impacts these impairments for each particular group. Delineating particular areas of weakness (e.g. initiation) is relevant for understanding more basic cognitive processes, as well as for developing targeted interventions.

**108.087 87** No Sex Differences Found in Autism Phenotype as Measured By the ADOS in Young Children with ASD. L. Huang-Storms*[1], S. Duvall[1], N. B. Knoble[2], A. P. Hill[1] and E. Fombonne[1], (1)*Oregon Health & Science University*, (2)*Oregon Health & Science Univeristy*

Background: The ratio of boys to girls diagnosed with Autism Spectrum Disorder (ASD) is estimated to be 4.3:1. Although epidemiological studies consistently find male predominance of ASD, few studies have explored sex differences in its clinical presentation.

Objectives: To evaluate sex differences in measures of the autism phenotype in a large sample of children with ASD.

Methods: Data was collected from 18 Autism Treatment Network (ATN) sites between the years 2007 and 2013. The Autism Diagnostic Observation Schedule (ADOS) Module 1 (preverbal/single words) was examined for 2,585 subjects included in the registry.

Results: There were 2,585 children in the sample (2,162 boys [83.6%]; 423 girls [16.4%]). There was no statistically significant difference in the gender repartition across ATN sites. The mean age at assessment was 4.28 years (SD=2.4) with no difference between boys and girls. No difference was found with respect to race (Caucasian, Black, Asian, "Other"), ethnicity (Hispanic, Non-Hispanic), or parent education ($p>0.10$). Mean algorithm total scores did not differ between boys and girls for Social Affect (14.58 vs. 14.67; $p>.50$), Restricted and Repetitive Behaviors (4.41 vs. 4.36; $p>.50$) or Total scores (18.99 vs. 19.03; $p>.50$). Similarly, no differences between boys and girls emerged for calibrated severity scores for Social Affect (7.12 vs. 7.10; $p>.50$), Repetitive Restricted Behaviors (7.62 vs. 7.56; $p>.50$) and Total (7.27 vs. 7.26; $p>.50$). Further analyses of 29 ADOS Module 1 individual item scores showed no differences for 27 items. Two non-algorithm items (Imagination/Creativity and Overactivity) showed slightly lower scores for girls than boys ($p=.03$), but the magnitude of differences was small and could have arisen due only to chance.

Further comparisons of the sample were performed by stratified age bands (< 3 years [N=877; 17.4% girls]; 3 to < 4 years [N=735; 16.3% girls]; 4 to <5 years [N=415; 16.6% girls]; and 5 years or more [N=558; 14.5% girls]) for the 3 algorithm scores and the 3 calibrated severity scores. Of these 24 additional comparisons, only one (girls in the 3 to < 4 years group) had marginally higher Social Affect algorithm scores (14.97 vs. 14.14; p=.04), a finding that could reflect chance alone.

Conclusions: Core features of the autism phenotype as measured by the ADOS Module 1 were strikingly consistent between boys and girls in this large sample of children. It is generally suggested in the literature that typically developing preschool-aged girls demonstrate more advanced social skills (e.g., social competence and social cognition) and communication skills (e.g., verbal abilities and gestures) than their male peers. This developmental difference was not found in the study sample, implying that young girls with ASD may be more impaired as compared to their same-sex typical peers than boys with ASD. Follow-up analyses will assess whether this pattern is also found for children with higher language levels administered ADOS modules 2 and 3.

**108.088 88** No Sex Differences Found in Cognitive Ability in Children with Autism Spectrum Disorder. S. W. Duvall*, L. Huang-Storms, N. B. Knoble, E. Fombonne and A. P. Hill, *Oregon Health & Science University*

Background: The notably discrepant sex ratio in autism spectrum disorder (ASD) is a longstanding phenomenon. Previous research examining sex differences in cognitive abilities has varied over time, with fewer recent studies demonstrating significant sex differences.

Objectives: To evaluate possible sex differences in cognitive functioning in a large clinical sample of children referred diagnosed with ASD.

Methods: Data was gathered through 18 Autism Treatment Network (ATN) sites from 2007 to 2013. We included 2 samples in this analysis, which were derived from the assessment performed at the time of diagnosis: Sample 1) Mullen Scales of Early Learning (MSEL: 1,346 children, 1,117 boys (83%); and 229 girls (17%)), and; Sample 2) Stanford-Binet Intelligence Scales, 5$^{th}$ Edition (SB-5: 2,717 children, 2,306 boys (84.9%) and 411 girls (15.1%)).

Results: In Sample 1, the mean age at assessment was 3.46 years (SD=0.99) with no difference between sexes. There was a slight overrepresentation of girls among families who identified as Black or "Other" race (p=.03), but no differences for ethnicity (Hispanic or not) or parental education were found. No significant difference was found between sexes for MSEL composite total scores (59.4 vs 58.5; NS) nor for any of the 5 MSEL subscales (Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language, all p>.15). In Sample 2, the mean age at assessment was 7.26 years (SD=3.34) with girls being significantly younger than boys (6.9 vs 7.3; p=.025). No difference for race, ethnicity or parental education was observed. All children had an SB-5 Abbreviated Battery IQ (ABIQ), with no difference between sexes (83.2 vs 81.2; p=.10). For the subsample (N=753; 80.4% boys) with full SB-5 scores, no difference was found between boys and girls for Non Verbal IQ (NVIQ, 80.4 vs 80.0), for Verbal IQ (VIQ, 75.8 vs 77.4) or for Full Scale IQ (FSIQ, 77.2 vs 77.7). Similarly, no difference was found for any of the factors (Fluid Reasoning: 80.8 vs 82.9; Knowledge: 77.4 vs 79.6; Quantitative Reasoning: 83.8 vs 83.2; Visual-Spatial Processing: 82.9 vs 80.5; Working Memory: 78.8 vs 78.9; all NS). We performed further analyses on cognitive scores grouped in 5 levels of IQ: <50, 50 to 69, 70 to 84, 85 to 99 and 100 and over. In sample 1, the percent distribution for these 5 bands of MSEL scores was: 43.5, 37.5, 10.5, 5.1 and 3.3, with no sex difference ($chi^2$=5.3, 4 df; p=.26). In Sample 2, the percent distribution for the 5 IQ levels was respectively: 9.4, 20.8, 18.4, 23.9 and 27.5, with no sex difference ($chi^2$=3.9, 4 df; p=.42). Similar, non significant results were obtained for the subsample of 753 subjects with full SB-5 scores.

Conclusions: In this large sample of children with ASD in the United States, no sex differences were found in overall cognitive ability or any of the SB-5 or MSEL subscales; this held true even after grouping by cognitive ranges. These findings are consistent with more current research, which may suggest that differences noted in the earlier research may be related to evolving diagnostic criteria over time.

**108.089 89** Parental Scaffolding of Emotion Understanding in Children with Autism Spectrum Disorders: Relations to Emotion Regulation Abilities. L. Berkovits*[1], B. Caplan[1], A. Eisenhower[2] and J. Blacher[3], (1)*Department of Psychology, UCLA*, (2)*University of Massachusetts, Boston*, (3)*University of California - Riverside*

Background: While tantrums, "meltdowns," and other behavior problems have been studied extensively among children with autism spectrum disorders (ASD; e.g., Bauminger, Solomon, & Rogers, 2010; Mayes, et al., 2012), the underlying emotional dysregulation that often spurs these behavioral symptoms is not well understood. Furthermore, emotion dysregulation is closely related to social difficulties for typically developing children (e.g., Blandon, Calkins, & Keane, 2010; Eisenberg et al., 1993). However, factors that may contribute to improved emotion regulation abilities throughout development (e.g., emotional understanding; parent-child discussions about emotions) remain understudied within this population.

Objectives: Specific research questions addressed in this paper are: 1) how do parents attempt to scaffold children's understanding of emotions? 2) how do children respond to parental emotion scaffolding? and 3) to what extent does parental scaffolding of emotional understanding influence the development of children's emotion regulation abilities at a later time-point?

Methods: The current study examines emotion dysregulation in 4- to 7-year-old children with ASD (current N=111) using data obtained from a multi-site longitudinal study; this study utilizes data from two time-points, 9 months apart. Children's diagnoses were confirmed using the ADOS and all children exhibited an IQ ≥ 55. Parental scaffolding of emotional understanding was observed and coded during a parent-child interaction task, along with children's emotion-related comments during this task. This 8-minute interaction task consisted of parents and children reading wordless picture books in a set order. Emotion dysregulation (e.g., mood swings, difficulty recovering once upset, proneness to frustration and disruptive outbursts) was measured using parent-report on the Emotion Regulation Checklist (ERC; Shields & Cicchetti, 1995) and children's behavioral and emotional dysregulation was assessed using parent-report on the Dysregulation Profile of the Child Behavior Checklist (CBCL-DP; Achenbach & Rescorla, 2000, 2001; Althoff et al., 2010).

Results: Analyses with the first set of coded subjects (n=23) showed that parents exhibit a wide range of emotion-based comments while reading wordless picture books with their children (mean frequency = 18.96; range = 2 to 36). Children whose parents commented on emotions more frequently also exhibited significantly more emotion-related comments during the task ($r$=.46, $p$<.05). When looking at the quality of the scaffolding, parental use of high-level scaffolding (e.g., asking the child to identify clues to emotions or connecting the child's understanding to real-life experiences) was related to children's elaborations about emotions beyond a simple response ($r$=.53, $p$=.009), while lower-level scaffolding (e.g., labeling emotions, asking direct questions about emotions) was not. The coding process will continue through the remainder of the sample of 111 and additional analyses will explore the extent to which parental scaffolding and children's emotional understanding relate to children's emotion dysregulation and regulation abilities at an assessment conducted nine months later.

Conclusions: Emotion dysregulation is a key variable to consider in understanding the functioning of children with ASD. Examining ways in which parents scaffold children's emotional understanding may help explain variability in children's emotion regulation abilities and inform interventions to alleviate social and behavioral impairments for this population.

**108.090 90** Parental Stress and Style in Mothers and Fathers of Children with Autism Spectrum Disorders, Learning Disabilities and Emotional Problems. Y. Ozturk*, A. Bentenuto, N. Zanella and P. Venuti, *University of Trento*

Background: Parenting is a process which constitutes a key component in the child's life. In addition, children with special needs present several difficulties to the parents. Considering that every special need has its own unique features, these difficulties which parents experience may vary with respect to the type of special needs. Previous researches addressed how mothers are affected by the challenges of raising a child with Autism Spectrum Disorder (ASD). To date, the studies have not covered the comparison between parenting children with ASDs, children with

learning disabilities and children with emotional problems, in terms of parental stress and style.

Objectives: In this study, we are interested in comparisons between three groups of parents in parental stress and style. These groups are defined with respect to the children's diagnoses: (1) parents of children with ASDs, (2) parents of children with learning disabilities and (3) parents of children with emotional problems. Moreover, we focus on whether mothers and fathers differ in terms of parental stress and attitude within each group.

Methods: We examined 228 parents (114 mothers and 114 fathers) using the Parenting Stress Index-Short Form (Abidin, 1995), the Parental Style Questionnaire (Bornstein et al., 1996), and the Symptom Checklist-90-Revised (Derogatis & Lazarus, 1994).

Results: We found that the level of stress of fathers, related to some of the basic behavioral characteristics of children that make them easy or difficult to manage, was affected by the type of diagnosis of children. In addition, focusing on gender differences within each group of parents, we found statistically significant results within several scales of the Parenting Style Questionnaire. Interestingly, the gender difference was emerged in the Parenting Stress Index only between mothers and fathers of children with learning disabilities.

Conclusions: These findings highlight both similarities and differences between parents within three groups defined with respect to the children's diagnoses and also between mothers and fathers within each group. Results suggest the consideration these similarities and differences, and the importance of specific parental intervention programs.

**108.091 91** Percentile Norms for the Aberrant Behavior Checklist in ASD. A. J. Kaat*, L. Lecavalier and M. G. Aman, *The Ohio State University*

*Background:*

The Aberrant Behavior Checklist (ABC) is one of the most commonly used rating scales among youth with intellectual and developmental disabilities, including autism spectrum disorder (ASD). It was originally developed with adolescents and adults in residential facilities and has since been revised to be suitable for children and for those living in the community. The original factor structure with five ABC subscales (Irritability, 15 items; Lethargy/Social Withdrawal, 16 items; Stereotypic Behavior, 7 items; Hyperactivity/Noncompliance, 16 items; Inappropriate Speech, 4 items) has recently been supported in children with ASD. The Irritability subscale was the primary outcome measure in several pivotal multi-site drug studies which resulted in FDA indications for risperidone and aripiprazole in the treatment of irritability in ASD.

*Objectives:*

The objective of this study is to present normative data on the ABC subscales among youth with ASD, overall and separated by educational level (preschool, school-age, or adolescent), IQ (dichotomized at 70), and gender.

*Methods:*

Data were obtained on 1,796 youth with ASD between the ages of 2 and 18 years who participated in the Autism Treatment Network (ATN). The ATN is a network of 17 children's hospitals. The first parent-completed ABCs and demographic information were used for these analyses. Since the ATN database is clinical, IQ measures were not uniform across participants. Intelligence was dichotomized at 70 to capture children with or without intellectual disability. Descriptive statistics were calculated on ABC subscales, including measures of skew and kurtosis. Percentile norms are reported (due to the significant positive skew) based on various demographic characteristics.

*Results:*

Overall the mean Irritability subscale score was 12.8 (sd 9.6, skew .76, kurtosis -.04), Lethargy/Social Withdrawal was 10.0 (sd 7.8, skew .92, kurtosis .55), Stereotypic Behavior was 5.0 (sd 4.6, skew .887, kurtosis .07), Hyperactivity/Noncompliance was 18.7 (sd 11.4, skew .408, kurtosis -.67), and Inappropriate Speech was 3.7 (sd 3.1, skew .63, kurtosis -.43). A significant positive skew emerged on all subscales when separated into demographically-homogenous subgroups. As such, percentile norms and percentile-based T-scores were calculated overall and separated by educational

level (preschool, school-age, or adolescent), IQ (dichotomized at 70), and gender.

*Conclusions:*

Normative information is useful for determining how prevalent an individual's problem behavior score is. In situations where distributional score characteristics deviate from univariate or multivariate normality, percentile ranks may be more useful clinically. Many statistical analyses assume distributional normality but are robust against minor violations to this at a group level. Percentile rankings, however, allow clinicians to quantify the individual's behavior more accurately. It also has potential research applications. For example, if a study seeks to investigate clinically-significant irritability and requires a baseline score two standard deviations above the ASD mean (which would hypothetically be the 98$^{th}$ percentile), the researcher may use a cutoff of 32 on the Irritability subscale. However, the 98$^{th}$ percentile actually coincides with a raw score of 36. This and other potential applications are explored.

**108.092 92** Relationship Between Mental Age and Everyday Adaptation Reported By Teachers in Low Functioning Individuals with and without ASD. A. San José Cáceres*[1], K. L. Ashwood[2] and F. G. Happe[3], (1)*Denmark Hill*, (2)*Institute of Psychiatry*, (3)*Institute of Psychiatry, King's College London*

**Background:**

Adaptive skills have been defined as key to the later outcome of individuals with ASD (Sparrow et al. 2005). However, individuals with ASD experience difficulties in everyday life regardless of cognitive ability (Black et al. , 2009). Contrary to TD, where IQ is closely related to adaptive skills, in ASD there seem to be a discrepancy between measures (Bolte & Poustka, 2002). In the case of individuals with Intellectual disability (ID) associated to ASD, IQ has been reported higher than adaptive skills (Perry et al., 2009) although adaptive skills remain more impaired than in the case of individuals with ID alone (Bolte & Poustka, 2002). In terms of mental age, individuals with ASD+ID present a distinctive adaptive profile (high motor skills, followed by daily living communication, and social skills; Perry et at., 2009). Although this profile was also reported for ID alone individuals, authors found significant differences between groups, concluding that ASD+ID individuals are socially impaired on adapting to everyday life over and above individuals of similar mental ages but not ASD. Teachers are a valuable source of information as the school is a very rich socio and educational environment. To date, no study has explored IQ/Mental Age in relation to adaptive skills as reported by teachers.

**Objectives:**

To examine the intelligence and developmental level of individuals with ID, with and without ASD, in relation to adaptive skills as reported by teachers reports. To explore whether the profile described by Perry and colleagues (2009) is replicated in relation to low-functioning individuals.

**Methods:**

Data was gathered from a sample of 33 individuals with ASD+ID and 37 individuals with ID alone (age range 5 -17) matched in Performance and Verbal MA, obtained from the Ravens Coloured Progressive Matrices (RPCM), and the British Picture Vocabulary Scales (BPVS) respectively. Adaptive skills were measured using the Vineland Adaptive Behaviour Skills Teacher Rating Form (VABS, Sparrow et al., 2006).

**Results:**

IQ comparisons were not possible due to the high number of individuals with IQ below basal scores (n = 20), or who fell outside the IQ age range (n = 17). VMA correlated significantly in ID with the social sub-domains of the VABS (all $r > .53$; all $p < .001$), but only interpersonal relationships for individuals with ASD+ID ($r = .54$, $p = .001$). PMA correlated significantly in ID with Living Skills School and socialization interpersonal ($r > .64$, $p < .001$) but not in ASD+ID.

**Conclusions:**

Results show a very distinct profile in the adaptive skills of individuals with ID with and without ASD. In ID, VMA play an important role on adaptive skills in general, while academic, school, and social interpersonal relationships are also mediated by PMA. In the case of ASD+ID, mental age seemed to be associated with academic skills, and VMA specifically to the relationships with others. The results here presented show how the socialization impairment characteristic of ASD

may result in a significant adaptability deficit – measured from teacher ratings - beyond their intellectual disability.

**108.093 93** Self-Concept and Psychosocial Adjustment in Adolescent Siblings of Individuals with ASD. L. A. Pepa*[1] and S. L. Harris[2], (1)*Rutgers University- Douglass Developmental Disabilities Center*, (2)*Rutgers University*

Background: Self-concept can be defined as a collection of ideas about the self (McConnell, Shoda, & Skulborstad, 2012). The structure of self-concept, as measured by self-complexity, can be broken into two factors: the number of roles one identifies as being important to the self, and the distinctness of these roles (Linville 1985; 1987). Research has suggested that high total self-complexity, and high positive complexity, is seen as a protective factor. Conversely, high negative complexity is considered a risk factor. These self-attributions originate at a young age, and are formed through social mechanisms, such as social feedback and social comparison. In this way, significant relationships, including family, have an important role in shaping an individual's self-concept. While much of the literature has focused on the influence of parents, research also suggests that siblings are significant figures. However, when an individual with autism is introduced into the family unit, the sibling relationship is significantly changed. This results from decreased social feedback and increased family stress, which may influence the formation of self-concept.

Objectives: The present study looked at the self-concept and psychosocial adjustment of 15 adolescent siblings of individuals with autism (ASD group) and compared this to the self-concept of 18 adolescents with a neurotypical sibling (Control group).

Methods: Study participants wereasked to fill out questionnaires related to their overall well-being, including measures of depression symptoms, social support, negative life events, and the sibling relationship.

Results: Results suggested that siblings in the ASD group fared as well as siblings in the Control group. They did not significantly differ on depression scores, social support, negative life events, or general self-complexity. There was some differentiation in sibling self-concept, with the ASD group showing more distinct sibling roles. Further, the findings of the present study supported the hypothesis that high negative self-complexity is positively related to depression scores. Lastly, it was found that distinctness among roles had a positive relationship with depression in the clinical group.

Conclusions: This study yielded important information about siblings of individuals with autism, and adolescent self-concept more generally. This supprts the line of research that suggests typical psychosocial adjustment and self-concept in siblings of individuals with ASD. Further, this provides support for the relationship between a highly negative self-concept and negative outcomes.

**108.095 95** The Differential Ability Scales-Second Edition and Cognitive Profile Variability in Young Children with Autism Spectrum Disorder. E. S. Mitchell*, C. Klaiman, M. Lense and S. Hoffenberg, *Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*

Background: There has been longstanding interest in elucidating the relationship between intellectual functioning and autism spectrum disorder (ASD), with particular interest in better understanding whether there is unevenness in the cognitive abilities of children with ASD (Joseph, Tager-Flusberg, & Lord, 2002). The Differential Ability Scales, Second Edition (DAS-II; Elliot, 2007) has been specifically recommended as a measure of cognitive abilities in children with ASD because the subtests' conceptually homogenous clusters allow for a clearer comparison of abilities and there are fewer language demands than with measures such as the Wechsler scales (Saulnier & Ventola, 2012). While the DAS-II holds promise as a useful assessment measure, there have been no published studies to date describing the DAS-II cognitive profiles of young children with ASD.

Objectives: To examine DAS-II cognitive profiles in young children with a diagnosis of ASD.

Methods: A record review was conducted of 145 diagnostic evaluations of children seen through a large outpatient autism center in a metro area. For inclusion in the present study, the evaluation had to include the DAS-II, Lower Early Years core subtests (Verbal Comprehension, Naming Vocabulary, Picture Similarities, and Pattern Construction) and a confirmed ASD diagnosis based on the results of a structured autism diagnostic interview and the Autism Diagnostic

Observation Scale. A total of 68 children ranging in age from 36 to 70 months (M=52.9, SD=9.7) met these criteria. Proportions of the sample with Verbal-Nonverbal (V-NV) discrepancies were identified based on the 13-point difference between Verbal and Nonverbal cluster scores required for significance at the .05 level of probability, as specified in the DAS-II normative data tables manual. In addition to V-NV discrepancies, subtest score patterns were examined within each cluster.

Results: Analysis of the V-NV cluster scores resulted in the following categories: 41% exhibited a significant discrepancy in favor of nonverbal abilities (V < NV), 12% exhibited a significant discrepancy in favor of verbal abilities (V > NV), and 47% exhibited no discrepancy (V = NV). Therefore, 53% of children demonstrated a significant discrepancy and the majority of the discrepancies were in the V < NV direction. The frequency of the V-NV discrepancies in this sample was significantly higher than reported for the DAS-II normative sample based on an exact binomial test, $p < .001$. In addition, a repeated measures ANOVA demonstrated significant unevenness in performance across subtests, $F(3, 201) = 12.1$, $p < .001$. The mean score for Verbal Comprehension was significantly lower than for all other subtests.

Conclusions: The present study documented cognitive profile variability on the DAS-II in a clinically referred sample of young children with ASD. The high frequency of uneven cognitive development suggests that the DAS-II may be a useful tool in differentiating patterns of cognitive strengths and weaknesses in ASD. Ultimately, the identification of these specific patterns in cognitive functioning is critical in young children, as it informs educational goals, intervention strategies, and progress monitoring.

**108.096 96** The Effects of Conducting a Functional Analysis on Problem Behavior in Other Settings: The Possibility of Interaction Effects. A. R. Reavis*, N. Call, S. Clark and N. Parks, *Marcus Autism Center & Children's Healthcare of Atlanta*

Background:

Children with autism may develop problem behaviors such aggression or self-injury that can result in harm to themselves or others. Studies have shown that basing treatments for severe problem behaviors upon the results of a prior functional analysis (FA) results in better outcomes (Campbell, 2003). Despite its standing as one of the most well supported guides to treatment of problem behaviors, it has been suggested that reinforcing problem behavior during FAs may result in an increase in problem behavior outside the FA setting. Call et al. (2012) and Shabaini et al. (2013) assessed whether problem behavior outside the setting in which an FA was conducted would increase when the FA was initiated. Results of both studies demonstrated that it was possible for problem behavior in the non-FA setting to be influenced by conducting a FA. Additionally, results of the Call et al. study suggested that increases and decreases in problem behavior outside the FA setting were both possible.

Objectives:

The purpose of the current study was to examine the influence of conducting an FA on problem behavior outside the FA setting while controlling for the presence of motivating events most likely to evoke problem behavior.

Methods:

Nine individuals with autism or related disorders participated while receiving services in a day-treatment clinic that specialized in the assessment and treatment of problem behavior. Participants' time while present at the clinic was divided into time spent in the *FA setting* or on the *unit*, defined as all spaces outside the FA setting. The rate of problem behavior that occurred on the unit served as the primary dependent variable.

Three probes were conducted each day on the unit. During each probe, the participants were exposed to at least one of the antecedents and associated consequences consistent with those evaluated within a test condition of the FA; demands, restricted attention, or restricted access to preferred tangible items.

There were two experimental conditions. *Baseline* occurred during the time between the beginning of the participants' admission and the initiation of the FA. During the *Functional Analysis* condition, an FA was conducted and included tangible, attention, demand, and toy play conditions. Problem behavior that occurred in the FA setting was reinforced on an FR1 schedule. Every third

instance of problem behavior that occurred on the unit was reinforced during the baseline and functional analysis conditions.

Results:

Overall, different effects of conducting an FA were observed across participants. For three participants, rates of problem behavior increased on the unit after the FA was introduced in the session room, for another participant problem behavior decreased on the unit after the FA was introduced, and for the remaining five participants, there was little to no change in the rate of problem behavior on the unit.

Conclusions:

The results of this study suggest than an FA, and the accompanying schedule of reinforcement for problem behavior, are capable of influencing problem behavior in a setting other than the one in which an FA is conducted.

**108.097 97** The Impact of Siblings on the Clinical Presentation of Children with Autism Spectrum Disorders. D. A. Zachor*[1], H. Hochman[2], A. Ben Avraham[2] and E. Ben Itzchak[3], (1)*Tel Aviv University / Assaf Harofeh Medical Center*, (2)*Ariel University*, (3)*Ariel University Center/ Assaf Harofeh Medical Center*

Background:

Sibling relationships may influence a child's development through close interaction, role-playing and sharing of emotions and experiences. These relationships might affect the younger and the older siblings differently. It is well accepted that older siblings may influence their younger siblings' development by serving as role models. Previous studies reported that positive sibling relationships may facilitate social development of children with autism spectrum disorders (ASD).

Objectives: The current study examined the impact of younger/older siblings on the clinical presentation of children with ASD.

Methods:

The study included 528 participants, 462 boys and 66 girls, with ages ranging from 18 to 60 months (M=33.1m, SD=11.1), diagnosed with ASD. Data regarding the number of siblings and their order in the family was obtained from the parents. Of the entire ASD group, 145 participants did not have a sibling, 116 had one or more, younger siblings, 215 had one or more, older siblings, and 52 had both younger and older siblings. The participants underwent assessments of autism severity, cognitive ability and adaptive skills. Autism symptoms severity was measured using the ADOS social-affect (SA) and restrictive and repetitive behaviors calibrated severity scales, and ADI-R algorithm scores in all domains. Level of adaptive skills was measured using the Vineland Adaptive Behavior Scales (VABS) composite standard scores.

Results:

Regarding autism symptoms severity, the ADOS SA severity scores were significantly lower in the ASD group with siblings in comparison to the group without siblings (p=.01). No significant differences were noted between the groups in ADOS RRB severity scores. In the same direction, parental report using the ADI-R algorithm scores revealed significantly lower scores in the communication domain for the group with siblings in comparison to the group without siblings (P=.001). No significant differences between the examined groups were noted in adaptive behaviors. We then examined the impact of the sibling order, older or younger than the index child, on the clinical presentation. The ADOS SA severity scores were significantly lower in the subgroup with only older sibling(s) (P=.003) and in the subgroup with only younger sibling(s) (P=.001) than in the group without siblings. In the same direction, the ADI-R algorithm scores were significantly lower in the communication domain for the subgroup with only older siblings (P=.002), and in the social and communication domains for the subgroup with only younger siblings (P=.013) than in the group without any siblings. The VABS composite scores were significantly higher only for the subgroup with younger siblings, but not for the subgroup with older siblings than for the group without siblings (P=.05). The positive effect of having either older or younger siblings on autism severity and adaptive skills disappeared in the subgroup with both older and younger siblings.

Conclusions:

For children with ASD, having either younger or older siblings may encourage social engagement with the sibling and may translate into better social interaction, communication and adaptive

skills. Future studies should look at other siblings' characteristics beyond age, such as gender and social abilities that might affect the clinical presentation in ASD.

**108.098 98** The Impact of the COMT Val158Met Polymorphism and Personality Traits on Social Responsiveness in Healthy Adolescents. L. Poustka*, *Central Institute of Mental Health*

Background: Autistic traits like deficits in social reciprocity are continuously distributed in the general population. Geneti, biological and psychological backgrounds of these traits in neurotypical individuals are still not well understood. Dopaminergic gene variants were reported to have an influence on prosocial behaviours.

Objectives: To investigate the potential role of a dopaminergic candidate polymorphism, the COMT Val158Met SNP for social reciprocity alongside with personality traits and internalizing problems.

Methods: 469 adolescents from a large international sample were genotyped for and assessed with the Social Responsiveness Scale (SRS), the NEO-Five Factor Inventory (NEO-FFI), and the Strengths and Differences Questionnaire (SDQ). An analysis of variance and a hierarchical multiple regression model were calculated to test the impact of COMT, personality and internalizing problems on social responsiveness.

Results: Carriers of at least one Val allele showed significantly lower SRS scores (p=.008) compared to those without a Val allele, indicating less social impairment in Val carriers. Also agreeableness and extraversion were negatively related to SRS scores, while for neuroticism and emotional problems, a positive association was found. All predictors together explained 20.6% of the variance of the SRS total score. **Conclusions:** Results suggest that the Val allele, representing catabolism of dopamine, alongside with personality dimensions is related to social reciprocity in healthy populations

Conclusions: Results suggest that the Val allele, representing catabolism of dopamine, alongside with personality dimensions is related to social reciprocity in healthy populations.

**108.099 99** The Relationship Between the Childhood Autism Rating Scale- Second Edition and Clinical Diagnosis Utilizing the DSM-5 and the DSM-IV. T. Dawkins*, A. T. Meyer and M. E. Van Bourgondien, *University of North Carolina*

**Background:** *The Childhood Autism Rating Scale, Second Edition* (CARS2; 2010) includes two rating scales- CARS2-Standard Version (CARS2-ST; formerly titled CARS) and the newly developed CARS2-High Functioning version (CARS2-HF). The CARS2-ST maintains the integrity of the CARS from 1988, and as such is considered "the strongest, best documented, and most widely used clinical rating scale for behaviors associated with autism" (Lord & Corsello, 2005). The CARS-ST is for use with children less than age 6 or over age 6 with an estimated IQ score of 79 or lower or with notably impaired communication. The original CARS (CARS2-ST) has been shown to have good agreement with the DSM-III-R, though it was somewhat over-inclusive compared to strict criteria (Van Bourgondien, et al., 1992). Many subsequent studies reported good to excellent agreement between the original CARS (CARS2-ST) and clinical diagnosis using DSM-IV criteria (Perry et al., 2005; Sponheim & Sparkland, 1996). In the CARS2 verification study and national field trials, the CARS2-ST had a sensitivity of .88 and a specificity of .86 compared to clinical diagnoses at the time of DSM-IV. For the CARS2-HF, the sensitivity was .81 and the specificity was .87.

**Objectives:** To assess the specificity and sensitivity of the CARS-2 when compared to DSM-IV versus DSM-5 criteria for ASD within a community based clinic sample.

**Methods:** Each participant was seen for a diagnostic evaluation at one of 5 community based TEACCH Centers that are part of the University of North Carolina TEACCH Autism Program (TEACCH). The assessments included administration of the CARS2, the Autism Diagnostic Observation Schedule-2 (ADOS-2), and a developmental history interview. All diagnostic conclusions were made on the basis of direct assessment and observation as well as developmental history. In addition, clinicians rated symptoms of autism on both the DSM-IV-TR and DSM-5 criteria for autism on the day of the diagnostic. Preliminary evidence was obtained for 68 participants using the CARS2-ST and 76 participants using the CARS2-HF. These participants are representative of a variety of socioeconomic and racial backgrounds from both rural and urban centers throughout the state. The TEACCH Centers conduct diagnostic evaluations

on all ages from toddlers through adults. Thus, the age range of participants rated on the 1.09 to 18.09 (mean= 4.39 years; SD= 2.85) for participants rated on the CARS2-STand CARS2-HF was 5.03 to 45.05 years (mean= 13.75 years; SD= 8.20).

**Results:** In preliminary analyses, the sensitivity of CARS2-ST was .74 and .78 across DSM-IV and DSM-5 respectively. The specificity of CARS2-ST was 1.00 across DSM-IV and DSM-5 criteria. The sensitivity of CARS2-HF was 1.00 across DSM-IV and DSM-5 while the specificity was .88 and .77 respectively.

**Conclusions:** Preliminary findings suggest that a high proportion of individuals who meet clinical cut-off for autism on the CARS-2 meet criteria for autism based on DSM-IV and DSM-5 criteria. The relationship between CARS2 ratings and different diagnostic subgroups (e.g. PDD, Anxiety, ADHD, etc.) will be presented.

**108.100 100** Using Parental and Teacher's Ratings for Differential Screening of Taiwanese Children with Higher Functioning Autism Spectrum Disorder from Children with Attention-Deficit/Hyperactivity Disorder. C. C. Chao* and I. H. Wu, *University of Taipei*

Background: Past research and clinical reports have revealed similarities in the symptomatic and behavioral characteristics between children with higher functioning autism spectrum disorder (HFASD) and those with attention-deficit/hyperactivity disorder (ADHD). Children with either diagnosis not only experience difficulties in social information processing, interpersonal relationships, attention, home and school adjustment, but also display oppositional behaviors and emotional problems. These behavioral similarities and overlapping symptoms make it difficult to differentiate HFASD and ADHD in clinical practice or even result in misdiagnosis, causing inappropriate or delayed treatments. Chao et al. (2013) have examined the validity of seven commonly used behavior rating scales in differentiating HFASD and ADHD children. They have found that either measure for general psychopathology, for specific symptomatology, or for social reasoning/functioning could significantly differentiate clinical groups (HFASD and ADHD) from typically developing (TD) comparison group. However, only two ASD symptom measures could differentiate HFASD from ADHD, i.e., the Gilliam Asperger's Disorder Scale and the Australian Scale for Asperger's Syndrome.

Objectives: To examine the utility of parental and teacher's ratings on behavior rating scales for differential screening of Taiwanese HFASD and ADHD children.

Methods: From August 2011 to November 2013, three groups of Taiwanese school-age (1$^{st}$ -6$^{th}$ grade) children were recruited to participate in this study, including: (1) children with HFASD (n=31), (2) children with ADHD (n=33), and (3) TD children (n=20). A comprehensive assessment protocol and indices were developed and cross-validated for differential screening of HFASD and ADHD. Five measures were used: (a) Child Behavior Checklist (CBCL)/Teacher Report Form (TRF), (b) Checklist for Autism Spectrum Disorder (CASD), (c) Gilliam Asperger's Disorder Scale (GADS), (d) the 4$^{th}$ Edition of Swanson, Nolan and Pelham Questionnaire (SNAP-IV), and (e) Socialization subscale of Vineland Adaptive Behavior Scale (VABS). All measures were employed to evaluate all the participating children by their parents and teachers. All the parental ratings and teacher's ratings were compared across three groups.

Results: Five parent-rated measures were found to differentiate the clinical groups from the TD group (i.e., CBCL, CASD, GADS, SNAP-IV, VABS) and two of which (i.e., CASD, GADS) could differentiate between HFASD and ADHD group. Likewise, five teacher-rated measures could differentiate the clinical groups from the TD group (i.e., TRF, CASD, GADS, SNAP-IV, VABS) and two of which (i.e., CASD, GADS) could differentiate HFASD from ADHD group.

Conclusions: Parental and teacher's ratings are useful in differentiating HFASD and ADHD from TD group. However, measures of general psychopathology or ADHD symptoms fail to differentiate HFASD from ADHD effectively. Only the behavior rating scales that assess ASD symptoms specifically is the most effective measures in differentiating HFASD and ADHD. Therefore, it is suggested that information regarding ASD symptoms should be routinely collected from parents and teachers when making differential diagnosis of HFASD and ADHD. It might also be helpful for special education teachers or school counselors to use ASD

symptoms rating scales as a screening tool in initial assessment for high-risk children.

**108.101 101** Validation of Eye-Tracking Measures of Social Disability As a Treatment Endpoint in School-Age Children with ASD. A. R. Wrencher*[1], J. Moriuchi[1], A. Klin[2], S. Shultz[3] and W. Jones[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

**Background:** One critical goal of biomedical research in autism is to develop effective treatments that improve the quality of life for individuals on the autism spectrum. Two major obstacles currently hinder this goal, particularly for the development of treatments that target core social deficits of the condition: the heterogeneity of the autism spectrum and the social nature of the disability. The heterogeneity means that different individuals will present with varying levels of affectedness, requiring different treatment approaches; and the social nature of the condition means that the disability itself is inherently challenging to quantify. Given these obstacles, two important questions present themselves: How do we best quantify the degree of social disability at the core of autism? And how do we best measure whether a treatment for social disability has been effective? The goal of the current research project is to test the extent to which eye-tracking measures of social disability can serve as successful endpoints or "outcome measures" for the assessment of new treatments.

**Objectives:** This study aims to assess the psychometric validity of eye-tracking measures to be used as treatment endpoints in school-age children with ASD.

**Methods:** We assessed the use of eye-tracking measures, which were collected during free viewing of naturalistic videos of social interaction in terms of their general appropriateness to the condition; their content, construct, and convergent validity; their reliability, precision, and internal consistency; as well as their interpretability and patient acceptability. To assess the range and distribution of scores found in the general population, we collected normative eye-tracking data from typically developing children (TD, mean age=9.61 years, N=42) and then also collected comparison values in a large and heterogeneous sample of children with ASD (mean age=10.55 years, N=128).

**Results:** Consistent with previous research, children with ASD spent significantly less time looking at the eyes than did TD peers (M(SD) = 32.3(17.8)% for ASD vs. 39.9(18.2)% for TD, $F$ = 51.8, $p$<0.05). Eye-looking reliability measures indicate good test-retest correlation within each group: $r$ = 0.619 for TD and $r$ =0.624 for ASD. The measures were collected with a greater than 88% success rate and with measurement accuracy of less than 3 degrees of visual angle.

**Conclusions:** Eye-tracking measures of visual scanning, while watching naturalistic scenes of social interaction, can serve as effective and valid quantifiers of social disability. In the current analyses, we focused on attention to the eyes of others; however, we expect that a more important assay of social disability will be measuring not only overall looking time to others' eyes, but more temporally sensitive measures of looking to the right eyes at the right moments in time. Our rigorous assessment of promising eye-tracking measures will provide us with multiple dimensions with which to quantify social deficits in a naturalistic way and assess the effectiveness of treatments. By doing so, we hope to alter the course of ASD so as to afford individuals on the spectrum an improved quality of life.

## 109 Repetitive Behaviors and Interests

**109.102 102** Sensory Problems in Parents of Children with Autism Spectrum Disorders (ASD). M. Uljarevic*[1], M. Prior[2] and S. R. Leekam[3], (1)*Wales Autism Research Centre, School of Psychology, Cardiff University, Cardiff, United Kingdom*, (2)*University of Melbourne*, (3)*Cardiff University*

**Background:** Previous research has shown that sensory problems are very prevalent in both individuals with ASD (Leekam et al., 2007) and their siblings (De La Marche et al., 2012). Surprisingly, despite this evidence and the inclusion of atypical reactions to sensory stimuli in the DSM-5 criteria for ASD, the frequency of sensory problems has not yet been examined in parents of individuals with ASD. Sensory problems are known risk factors for affective disorders, both in ASD and the general population. Given the high rate of affective disorders in parents of children with ASD, investigating sensory symptoms in parents is important both from clinical and theoretical stand points.

**Objectives:** 1) To explore the frequency of sensory problems in mothers of children and adolescents with ASD; 2) To investigate whether sensory problems were associated with the Broader Autism Phenotype (BAP) Traits.

**Methods:** 50 mothers of children and adolescents with ASD were recruited to the study. None of the mothers had diagnosis of ASD. Mothers were asked to complete the Adult Sensory Profile (AASP; Brown & Dunn, 2002). The AASP is a norm-referenced questionnaire that provides scores for four types of responses to sensory stimuli (sensory quadrants): hypo-sensitivity, hyper-sensitivity, sensation seeking, and avoiding. The manual provides scores from a large normative sample of typically developed adult individuals. The Interpersonal Reactivity Index (IRI; Davis, 1994) was used as a proxy for Broader Autism Phenotype (BAP) traits.

**Results:** The scores of mothers of children with ASD were compared with norms provided by AASP manual. 62% of mothers had higher sensory hypo-sensitivity scores than TD norms (36% had scores between 1 and 2 standard deviations (SDs) above the mean, and 26% 2 or more SDs above the mean), 44 % had higher scores for sensory sensitivity (14% between 1 and 2 SDs and 30% 2 or more SDs above the mean). 48% had higher scores for sensory avoidance (22% between 1 and 2 SDs and 26% 2 or more SDs above the mean). Interestingly, 60% of parents had lower sensory seeking scores than TD norms (30% between 1 and 2 SDs and 30% 2 or more SDs below the mean). None of sensory scores were associated with BAP (as indexed by IRI).

**Conclusions:** This is a first study to investigate sensory problems in parents of children with ASD and our findings suggest that these problems are indeed very frequent. These results have important theoretical and clinical implications. Since sensory problems have been found to be associated with affective disorders in both ASD and general population and affective problems are indeed prevalent in the parents of children with ASD, future work will need to address the role of sensory problems in the development and maintenance of anxiety in parents of ASD individuals. Furthermore, recent studies suggest a degree of heritability of sensory problems in the general population (Goldsmith et al., 2006) and further work needs to be done to elucidate the contribution of genetic and environmental influences on the expression of sensory problems in ASD.

**109.103 103** Subtypes of Restricted and Repetitive Behaviors in Minimally Verbal Children with Autism Spectrum Disorders. C. T. Moody*[1], R. M. Jones[1], S. L. Bishop[2] and C. Lord[1], (1)*Weill Cornell Medical College*, (2)*Center for Autism and the Developing Brain, Weill Cornell Medical College*

Background: Restricted and repetitive behaviors (RRBs) are a core feature of the autism phenotype. Research analyzing the factor structure of the RRB items on the ADI-R has provided evidence for at least two RRB subcategories: repetitive sensory motor (RSM) and insistence on sameness (IS) behaviors (Cuccaro et al., 2003; Szatmari et al., 2006; Richler, Bishop, Kleinke & Lord, 2007). Alternatively, factor analyses of the Repetitive Behavior Scale Revised (RBS-R) have primarily supported a five-factor model of RRBs: Sensory-Motor, Self injury, Compulsive, Ritualistic/Sameness, and Restricted Interests (Lam & Aman, 2007). Recently, Bishop et al. (2013) examined relationships between the factors of the ADI-R, factors of the RBS-R, and other child characteristics. The ADI-R RSM and IS factors were significantly correlated with the RBS-R Sensory-Motor and Ritualistic/Sameness factors, respectively. These pairs of matched factors exhibited similar relationships with other child variables as well. These findings support the construct validity of the RSM and IS subcategories of RRBs in ASD. However, because studies examining the RSM and IS subcategories have utilized larger, more heterogeneous samples of children with ASD, it is possible that RRB subtypes organize differently in specific groups of children within ASD (i.e., nonverbal children), and that these differences get lost in these larger samples.

Objectives: The primary aim of this study is to test whether RSM and IS scores on the RBS-R and ADI-R exhibit similar cross-measure relationships in a minimally verbal sample of children with ASD.

Methods: Participants will include at least 50 children (4-8 years of age) who enrolled in a randomized clinical intervention trial and were assessed prior to receiving treatment across four sites. All children were classified as minimally verbal through parent report and the use of a naturalistic language sample (<20 spontaneous

words in 20 minutes). ASD diagnoses were confirmed with the ADOS-2 and ADI-R, cognitive abilities were measured with the MSEL and Leiter-R, and parent report of restricted and repetitive behaviors were collected with the RBS-R.

Results: Data collection is ongoing. Preliminary analyses suggest similar relationships between the RSM and IS subscales on the ADI-R and RBS-R as in previously published papers (Bishop et al., 2013). ADI-R RSM scores were correlated with the RBS-R Sensory-Motor subscale ($r$ = 0.69); similarly, IS scores on the ADI-R were correlated with the RBS-R Ritualistic/Sameness subscale ($r$= 0.58). Subsequent analyses will confirm the presence of the RSM and IS factors within the ADI-R in this specific sample and further examine relationships between these factors and subscales on the RBS-R. Additional analyses will explore whether these subtypes of behavior are associated with other child variables in ways similar to those seen in larger samples.

Conclusions: If, as we anticipate, the results from this minimally verbal sample correspond to previously published findings, the current study will further support the validity of the RSM and IS subcategories of RRBs. If the factors do not exhibit relationships that are similar to those reported in previous studies, this would have implications for measurement of RRBs in children with low language abilities.

**109.104 104** Computerized Quantification of Hand Stereotypies and Postural Control. S. Goldman*[1], C. Terilli[1], B. Malcolm[1], A. B. Brandwein[2], J. J. Foxe[3] and J. S. Butler[3], (1)*Albert Einstein College of Medicine*, (2)*The Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory of the Children's Evaluation and Rehabilitation Center (CERC)*, (3)*The Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory, Albert Einstein College of Medicine*

**Background:** Motor abnormalities are highly prevalent in Autism Spectrum Disorders (ASD) yet they are poorly understood and have not been studied with the necessary fine-grained methodologies. These anomalies encompass different aspects of the motor system including gait, apraxia, hypotonia or stereotypies. Among these motor signs, postural control (PC) defined as dynamic body stability is, in fact the earliest diagnostic marker that differentiates ASD high-risk siblings from typically developing (TD) infants. Body stability is an essential component of motor development that requires attention and integration of multisensory inputs such as visual and somatosensory cues. In view of recent findings on sensory integration processes in ASD we sought to use virtual reality to assess PC and compared the performances of children with ASD with their matched TD peers. We used motion capture technologies to examine how the brain integrates sensory information during execution of movements. Another prevalent and highly stigmatizing behavior in ASD is repetitive purposeless hand movements called stereotypies. The unknown pathophysiology and the lack of objective measurements have made their treatment largely unsuccessful. Here we expand our previous work on characterization of stereotypies, using wireless child-friendly accelerometery technologies to quantify repetitive behaviors. We examined the effects of age, IQ, autism status, occluded vision and stereotypies on postural control.

**Objectives:** (1) assess motor development using a clinical battery (2) apply our experimental PC protocol (3) quantify stereotypies at the kinematic and physiological levels (4) test the hypothesis that ASD children with stereotypies show significant decrease in postural stability (larger sway area) and lower motor scores compared to matched TD children.

**Methods:** A battery of motor, cognitive and diagnostic assessments was administered to 6 children with ASD (mean age, 5 years 3 months) and their TD peers matched on chronological age and NVIQ. (a) Variability in sway area during PC tasks was recorded for a range of challenging postures through *Optitrack* and *Microsoft kinect* motion capture systems. Fourteen postures of 20 sec each alternating between eyes closed and eyes open were portrayed by a cartoon character and projected on a wall facing the child. (b) Hand stereotypies were video-recorded during a series of standardized activities and quantified using wireless wrist accelerometers.

**Results:** Preliminary analysis shows that TD children exhibit less body sway than children with ASD. Postural performance (e.g., standing on heels vs. standing on toes) differed between TD and ASD groups. The more challenging postures resulted in larger differences between the groups with eyes-closed postures resulting in larger sway in ASD than TD children. Developmental motor assessments revealed lower scores in the ASD

group for timed manual dexterity and complex motor coordination tasks. The 3-axis accelerometery data point to episodes of variable length of predetermined patterned movements of abnormally high frequency.

**Conclusions:** Preliminary results of reduced postural stability with occluded vision in ASD are consistent with reported underdeveloped postural control system. The quantifiable motor performances in children with ASD are in line with a neuronal-based model suggesting abnormalities in underlying cerebellar and basal ganglia networks and calls for further investigations.

**109.105 105** Effects of Environmental Enrichment on Repetitive Behaviors in the BTBR T+Tf/J Mouse Model of Autism. S. E. Reynolds*[1], M. Urruela[2] and D. P. Devine[2], (1)*Virginia Commonwealth University*, (2)*University of Florida*

Background: BTBR T+tf/J (BTBR) mice have recently emerged as a well-validated mouse model of autism due to their manifestation of core phenotypic autism behaviors: impaired socialization, deficits in communication and repetitive behaviors. While it is unknown whether BTBR mice share a cause of these altered behaviors with autism in humans, the collective manifestation of these symptoms provides a model in which treatment options may be explored in phenotypic behaviors of interest. Specifically the presence of both lower and higher order repetitive behaviors make the BTBR mouse a promising model for testing the effects of therapeutic interventions for the reduction of repetitive behaviors in autism.

Objectives: To evaluate the effectiveness of environmental enrichment for reducing repetitive behaviors in the BTBR mice. We hypothesized that housing in an enriched condition would reduce the number of higher and lower order repetitive behaviors seen in this strain.

Methods: All research was conducted in a laboratory setting at a research university; all procedures were approved by the institutional animal care and use committee. Subjects were 15 BTBR male mice and 16 control C57BL/6J (B6) male mice; mice from each strain were randomly assigned to either control or enriched housing. Lower order behaviors were captured by assaying the time and sequence of grooming, while higher order behaviors were measured using a pattern analysis of an object exploration task from digital recordings. Baseline scores were established at 7 weeks of age, followed by 30 days of housing in either standard or enriched cage. Baseline scores were compared between strains at baseline using T-tests; Post-tests scores were analyzed using a two-way analysis of variance which allowed us to examine differences based on strain, housing condition, and the interaction of strain x housing condition.

Results: As expected, BTBR mice spent significantly more time grooming and had more rigid grooming sequence than control mice at baseline. After 30 days of enrichment housing, BTBR mice demonstrated a significant reduction in time spent grooming, resulting in levels that were lower than those exhibited by BTBR mice in standard housing. No changes were seen in the rigidity of the grooming sequence. In contrast to previous findings, no differences were found for higher order repetitive behaviors between strains at baseline. Subsequently, enrichment did not significantly alter the number of higher order repetitive behaviors at posttest.

Conclusions: The results suggest that environmental enrichment may be beneficial for reducing the time spent engaging in lower order repetitive behaviors, but may not change the overall quality of the behaviors when they do manifest. Extracting information about human ASD from animal models must be done with caution. That said, our research supports a hypothesis that therapeutically engaging children with ASDs in stimulating sensory-motor activities may be beneficial in reducing some types of repetitive behavior.

**109.106 106** Examining the Effects of Jasper and Enhanced Milieu Teaching on Repetitive Behaviors and Scripted Language. E. A. Fuller*[1], J. Nietfeld[1], L. H. Hampton[1], A. P. Kaiser[1] and C. Kasari[2], (1)*Vanderbilt University*, (2)*University of California Los Angeles*

Background: Restricted and repetitive behaviors, interests, and activities (RRBs) are one of two core diagnostic features of autism spectrum disorder (American Psychiatric Association, 2013). RRBs define a broad category of behaviors, including motor stereotypies, unusual sensory preoccupations, and echolalia. RRBs have been shown to interfere with child learning (Koegel & Covert, 1972) and have been the focus of a broad range of behavioral interventions (Rapp & Vollmer, 2005). The current study examined the

extent to which RRBs change over the course of an intervention targeting social attention, play and spoken language, and the relationship between scripted language and social communicative utterances.

Objectives: 1) What is the relationship between parent-reported RRBs, the repetitive behavior score on the ADOS, and observed measures of RRBs? 2) Do these measures change over the course of intervention? 3) Over the course of intervention, does observed repetitive behavior decrease as language increases?

Methods: Twenty minimally verbal (less than 20 words) children diagnosed with ASD between the ages of 4.5 and 8 years old participated (16 males, mean age 6.39). The intervention used the strategies associated with JASPER/Enhanced Milieu Teaching (Kasari et al, submitted) to teach joint attention, nonverbal and verbal requests, and comments. Data were selected from the pre and post intervention assessments, approximately 3 months apart. The repetitive behavior subscale of the ADOS was measured pre-intervention, and parent-reported Repetitive Behavior Scale (RBS), social communicative utterances (SCU), and scripted language were measured pre- and post-intervention.

Results: Results show that there was not a significant correlation between ADOS repetitive behavior subscale and pretest RBS scores ($r=.202$, $p=.436$), or between ADOS repetitive behavior subscale and scripted language on the language sample at pretest ($r=.123$, $p=.606$). Over the course of intervention, while total social communicative utterance did show significant changes ($t = -2.3918$, $p = 0.02727$), RBS did not show significant changes from pretest to posttest ($t = 0.414$, $p = 0.684$). RBS remained low pre- and post-test (pre test mean=30.11, sd=20.27, post test mean=34.15, sd=24.23). Decreases in scripted language only approached significance ($t = 1.7147$, $p= 0.1027$). Changes in social-communicative utterances were not significantly related to changes in scripted language over the course of intervention ($r=.276$ $p=.239$).

Conclusions: There are several possible explanations for the nonsignficant findings. First parents rated their children as having low levels of RBS although observations during the ADOS suggested moderately high levels of repetitive behavior. Second, some children had extremely low rates of any language behavior during the language sample session, including both social communicative utterances and scripted language. These factors, combined with the small sample size, may have affected the outcomes. To further examine the functional relationship between behavior and language during the sessions, we are coding all repetitive behaviors, during the first two intervention sessions compared to the final two intervention sessions. We hypothesize that the inclusion of motor stereotypies as well as verbal scripts will provide a more representative data set to answer to the question of correlation between changes in observed RRBs and language over the course of intervention.

**109.107 107** Managing Repetitive Behaviours in Young Children with Autism Spectrum Disorder (ASD): New Parent Group Intervention. V. Grahame*[1], L. Dixon[1], J. Rodgers[2], D. Brett[2], H. McConachie[2] and A. S. Le-Couteur[2], (1)*NTW NHS Foundation Trust*, (2)*Newcastle University*

**Background:** Repetitive behaviours (RBs) can interfere with a child's ability to learn new skills and engage in daily living activities. Parents report that RBs interfere with family functioning and are among the most stressful behaviours to manage. However, not all RBs are problematic. It is important to help parents understand RBs and learn how to manage them early, with the aim of reducing the impact for child and family. Most ASD-specific early intervention programmes focus on social communication. Parents rarely receive specific advice about their child's RBs.

**Objectives**: This pilot randomised controlled trial (RCT) aimed to evaluate feasibility, acceptability and impact of a new 8-week group-based parent intervention which was developed in collaboration with parents of young children with ASD.

**Methods:** 45 families of children with ASD (3 to 8 years) were randomised to immediate or delayed intervention. The outcome measures include level of change in parent-chosen 'target' RB (independently rated); 'blind' researcher-coding of child and parent behaviours from video; parent questionnaires (RBQ2 and Self-Efficacy). Measures were taken at baseline, FU1 after 10 weeks, FU2 two months later, and FU3 two months later.

**Results:** At baseline, all children had high Autism severity (ADOS mean severity score 7.04; SRS total mean 120.13) and moderate-low adaptive functioning (VABS composite mean 68.76).

Parent attendance at groups was 96% overall. Parents who attended the group reported that they found the course helpful, and that that it increased their knowledge and confidence in managing RBs; e.g. "I feel more relaxed with dealing with RBs", "I am more confident, have a bank of strategies I can use".

A significant impact of intervention was found for RBQ2 factor 3 'preoccupation with restricted patterns of interest' (FU1, p= .04, $\eta_p^2$= .09; FU2, p= .02, $\eta_p^2$= .12; i.e., moderate to large effect sizes), and for factor 4 'unusual sensory interest' (p= .04, $\eta_p^2$= .10). There was a significant main effect of group on parent Self Efficacy (p= .02, $\eta_p^2$= .13); t-tests revealed that the immediate intervention group had higher self efficacy than the control group at FU1 and FU2. Analysis of observational measures of child RB and parent management strategies, rated level of improvement in parent–chosen target RB, and FU3 data will also be presented.

**Conclusions:** The results of this pilot RCT suggest that a parent group intervention for managing RBs in young children with ASD has potential for beneficial impact. Parents were willing to be recruited and randomised, the format and content of the groups were feasible and acceptable, and the outcome measures were appropriate for use in a future fully powered trial.

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**109.108 108** Mapping the Phenotype of Phelan McDermid Syndrome. A. M. Mieses*, T. Tavassoli, L. Bush and A. Kolevzon, *Icahn School of Medicine at Mount Sinai*

**Background:** Phelan McDermid Syndrome (PMS), also called 22q13 Deletion Syndrome, is caused by deletion or mutation of the *SHANK3* gene located at the terminal end of chromosome 22 (Durand et al., 2007). The *SHANK3* gene codes for a master scaffolding protein which forms a key framework in the postsynaptic density of glutamatergic synapses and plays a critical role in synaptic function (Boeckers et al., 2006). PMS is characterized by global developmental delays, severely delayed or absent speech, motor skill deficits, and autism spectrum disorder (ASD) (Soorya et al., 2013). The clinical presentation has been described in several case report series and some prospective analyses yet no study has comprehensively described the neurobehavioral phenotype.

**Objectives:** The aim of this study was to refine the ASD phenotype within PMS and preliminary results presented herein focus on the restricted and repetitive behavior domain.

**Methods:** Subjects were recruited as part of ongoing studies in PMS at the Seaver Autism Center at Mount Sinai. The following questionnaires were administered to caregivers of affected children in person, via telephone or mail: Aberrant Behavior Checklist (ABC; Aman et al., 1985); Repetitive Behavior Scale-Revised (RBS; Bodfish et al. 2000); Nisonger Child Behavior Rating Form (NCBRF; Aman et al., 1996); Sensory Profile (Dunn, 1999).

**Results:** Of 30 recruited subjects, 86.7% completed all parent questionnaires (56.7% male; mean age=10.8 years; SD=8.06). Results were compared to published samples in ASD or intellectual disability (ID). One-way analysis of variance (ANOVA) was performed for each domain on each assessment to determine whether there were significant differences between groups.

Results suggest that differences exist between children with PMS and those with ASD and/or ID with regard to restricted and repetitive behaviors. Specifically, children with PMS show: (a) less irritability, evidenced by lower mean levels of Irritability on the ABC ($p<0.003$); (b) fewer repetitive behaviors in all but one domain (Self-Injurious) on the RBS [Stereotypic and Ritualistic ($p<0.003$), Sameness ($p<0.03$), Compulsive and Restricted ($p<0.05$)]; (c) less anxiety according to the NCBRF Anxiety domain ($p<0.003$). No differences were observed in the following domains: (a) stereotypies on the ABC or NCBRF; (b) ritualistic behavior on the NCBRF; (c) self-injurious behavior on the RBS; (d) sensory reactivity or sensory seeking on the Sensory Profile.

Results for stereotypic and ritualistic behavior conflicted across instruments. The RBS suggested lower levels of stereotypic and ritualistic behavior in PMS compared to ASD while the NCBRF showed no difference compared to ID. This discrepancy may be due to the types of items included in the assessment of these domains across instruments and/or differences in comparison samples.

**Conclusions**: These results suggest that the ASD phenotype within PMS may be distinguished from idiopathic ASD and/or ID. Future studies will focus on refining the understanding of the social, cognitive, and language domains in PMS, and will explore whether a correlation exists between genotype and phenotypic severity. Characterizing the neurobehavioral phenotype in PMS is critical for developing appropriate assessment tools and outcome measures for use in treatment studies.

**109.109 109** Special Interests in Adults with and without ASD: A Comparison Study. K. Armstrong*[1], F. Shafai[2], I. Oruc[2] and G. Iarocci[1], (1)*Simon Fraser University*, (2)*University of British Columbia*

Background: Although restricted interests have been included as a diagnostic symptom of ASD since the disorder's original inclusion in the DSM, only a handful of studies have been conducted on the topic, with most focusing on the content of interests. This study investigated the quantitative components of interests.

Objectives: The goal of this study was to determine whether there were differences between adults with ASD and those without ASD who have special interests. Both groups had similar interest content in areas such as computer/video gaming, animals, sports, and anime/Japanese culture.

Methods: Twenty adults without ASD who were recruited for having a special interest (TD-SI group) which they self-identified being "obsessed" with, and eighteen adults with high-functioning ASD (ASD group) confirmed with the ADOS, reported on aspects of their interest including when it started, the duration, when it peaked, the percentage of time they *do* spend on their interests, the percentage of time they *would like*to spend on their interest, the amount of money they spend on their interest, and the number of people they share their interest with. Full scale IQ (FSIQ) was calculated based on the Wechsler Abbreviated Scale of Intelligence (WASI-II), and the Autism Spectrum Quotient (AQ) was used to obtain an estimate of ASD symptoms.

Results: A one-way ANOVA was used to test for differences between the ASD and TD-SI groups on the variables measured. There were no significant differences between the groups on age, and both groups had FSIQs in the average range. There was a significant difference in AQ scores (TD-SI $x$=17; ASD $x$=27), indicating the TD-SI group did not have high levels of ASD symptoms. On the interest variables measured, there were no significant differences between the groups for the age their interest started ($x$=10.5 years old for both groups), the duration of their interest (TD-SI $x$= 14 years; ASD x= 13 years), age their interest peaked (TD-SI $x$=17; ASD x=16), percentage of their spare time they *do* or *would like to* spend on their interest; ($x$~ 50% for both groups on both measures), or the amount of money they spend on their interest (TD-SI $x$=$52/month; ASD $x$=$54/month). Although not yet statistically significant (data collection is ongoing and $p$ is approaching significance) the groups did differ on the number of people they shared their interest with (TD-SI $x$=13 people; ASD $x$= 6 people).

Conclusions: The results indicate that interests in ASD are not atypical on the variables measured compared to those of TD peers who also have special interests except that they are less likely to share their interest with others. This may reflect that having better social skills allows you to be more social when pursuing your interest or that involving more people in your interest creates better social skills and/or opportunities. Further study is warranted to investigate the social components of interests and their impact on people with ASD.

## 110 Social Cognition and Social Behavior

**110.110 110** Reduced Recognition of Dynamic Facial Emotional Expressions in Children with ASD. K. Evers*, J. Steyaert, I. Noens and J. Wagemans, *KU Leuven*

**Background:** A vast number of researchers focused on the processing of facial emotional expressions in ASD, using a variety of paradigms and methodologies, and resulting in inconclusive and mixed findings. The Emotion Recognition Task is an emotion labelling task which already proved to be valuable in detecting subtle emotion recognition peculiarities in several clinical and non-clinical samples. Furthermore, this paradigm demonstrated its usefulness in identifying facial

emotion recognition impairments in adolescents with a clinical diagnosis of ASD and in non-clinical adults with ASD traits. Given that neurocognitive studies often examine school-aged children without an intellectual disability, it seemed important to extend the findings with the Emotion Recognition Task to that population. In line with the recent interest in a dimensional perspective on ASD and the search for endophenotypes, the relationship between demographic factors and emotion recognition was also evaluated.

**Objectives:** The aim of this study was to examine emotion recognition abilities in a large sample of children with and without ASD. Extending previous studies, we also wanted to investigate the relationship between participant characteristics – apart from diagnostic classification – and emotion recognition performance.

**Methods:** Emotion recognition abilities were measured with the Emotion Recognition Task, which is an often-used emotion labelling task with dynamic facial expressions of six basic emotions, namely anger, disgust, fear, happiness, sadness, and surprise. Two levels of emotional intensity were used: an intermediate and a high emotional intensity level. Performance was compared between 45 children with ASD and 50 typically developing children, group-wise matched on intelligence and age. Participants were aged 6 to 14 years and none of them had an intellectual disability. ASD traits were measured with the Social Responsiveness Scale (SRS) and empathy was measured with the Empathy Quotient (EQ).

**Results:** Results showed that the ASD group generally performed worse than the comparison group, and this impairment appeared emotion-specific: the ASD group was especially outperformed by the typically developing group when labelling sadness, disgust and surprise. However, the typically developing group performed better when identifying fear. Both groups were better at recognising high intensity expressions than intermediate ones. After correcting for response biases, the differential effect of emotions disappeared, but the overall poorer emotion recognition performance in the ASD group remained significant. Age nor intelligence were associated with emotion recognition. However, emotion recognition was correlated with SRS scores and EQ scores.

**Conclusions:** Extending previous work using the Emotion Recognition Task, we showed a poorer emotion recognition performance in 6-to-14-year old children with ASD. Moreover, we revealed that response biases could (partially) attribute to the emotion-specificity of their impairment. In addition, emotion recognition abilities were associated with ASD traits and empathy, such that children with higher ASD traits and lower empathy, had a poorer performance on the emotion recognition task.

**110.111 111** A Longitudinal Look at the Effectiveness of Teaching Social Thinking to Adolescents with Autism Spectrum Disorders. P. Crooke*, *Social Thinking*

Background: The recent surge of information about autism in the mainstream and professional literature has prompted new interest in treatments for individuals with Autism Spectrum Disorders (ASD). Unfortunately, research on the usefulness and effectiveness of novel approaches within this population has traditionally lagged behind the basic sciences, especially related to individuals with average to above average language and cognitive abilities. For those with complex language, social *cognitive* tasks, such as interpreting other's actions or intentions, understanding social reciprocity, and adjusting verbal/nonverbal behavior according to social cues, prove to be challenging (Koning & Magill-Evans, 2001; Ozonoff & Miller, 1995; Tsatsanis, Foley, & Donehower, 2004; Weiss & Harris, 2001). Studies addressing the effectiveness of treatments with a social emotional emphasis are key for all children and are most certainly a critical component for te ASD population. In fact, teaching basic social "skills" to those with strong language and cognitive skills only scratches the surface of broader social learning needs.

Objectives: The purpose of this study was to examine the effectiveness and long term outcomes of a social cognitive intervention (*Social Thinking*) in four 9-11 year old boys with Autism Spectrum Disorders (diagnosis of AS and HFA).

Methods: Four boys, aged 9-11 years, were included this treatment study. Multiple baseline measures across behaviors were used to examine generalization of social pragmatic and social problem solving skills immediately after an eight-week pilot intervention and one-year post intervention. All lessons within the treatment model were grounded in the principles of social

cognition (Social Thinking). The format of each treatment session included the following components: 1) **Gathering** (3-5 minutes of open talk time); 2) **Group lesson** (Specific social cognitive strategies/*Social Thinking* Lessons); 3) **Practice/Unstructured time.**Therapists provided verbal/visual feedback during the practice/unstructured time to reinforce the lesson. Weekly meetings and checklists addressed treatment fidelity and consistency. External validity and contextual relevance for families and subjects were highlighted.

Results: Findings indicated gains on dependent measures from baseline to generalization probes during the 8-week intervention as well as an increase or maintenance during a one-year follow-up probe. All four subjects either maintained or increased "expected" social behaviors or decreased "unexpected" social behaviors with the exception of *verbal initiations*. However, the change in this skill appeared to be a result of limited verbal demands during the activity included in the measure. Both parents and subjects indicated an increase in social awareness and problem solving strategies.

Conclusions: This study adds to the small pool of clinic-based studies examining the effectiveness social interventions based on social cognition. This model is a shift from traditional social skill approaches in that this cognitive behavioral approach (*Social Thinking)* promotes understanding of "why" related social skills are relevant in social exchanges and suggests that a meta-cognitive approach may be more relevant for those we currently refer to as AS/HFA or those with ASD who have strong cognitive and language skills.

**110.112 112** A Mixed Methods Study of Social Participation Patterns and Preferences of Children with Autism. L. Crabtree*, *Towson University*

Background: For all children, engagement in the occupation of social participation at home, in school and in the community is critical to healthy development. For children on the autism spectrum, social participation is especially challenging, due to core deficits in pragmatic language skills and understanding social cues. Social patterns and preferences of children with autism have not been identified, limiting effectiveness of programming and intervention outcomes.

Objectives: The purpose of this study was to explore social participation patterns and preferences from the perspectives of 8- to 12-year-old children with autism. This knowledge is important, as gaining children's perspectives provides insight into their values, preferences and motivations related to social participation, which can form the basis of optimal programming.

Methods: A concurrent triangulation mixed methods approach (Creswell & Plano-Clark, 2007) incorporated descriptive quantitative data and a qualitative case study design. The quantitative phase utilized the *Children's Assessment of Participation and Enjoyment* and the *Preferences for Activities of Children* (King, et al., 2004) to measure social participation patterns and preferences of 32 children with autism. Data were analyzed using descriptive statistics and t-tests. The qualitative phase incorporated interviews, drawings, and observations of social interactions to understand the perceptions of six of these children's experiences with and preferences for social participation occupations. Transcribed interviews and field notes were coded for emergent themes. A matrix of quantitative and qualitative data within each case facilitated constant comparative analyses across cases.

Results: Children in this study had significantly restricted access to social opportunities, primarily participating in activities with their family members and within the home environment. The children were interested in social activities with peers, despite having difficulty articulating strategies to do so. Their social participation patterns did not match their preferences for social activities. Younger children indicated greater preferences for social activities than did the older children. Girls (n=4) demonstrated different patterns than boys (n=28). Conflict with others, strict rule adherence, and limited opportunities emerged as barriers to social participation.

Conclusions: This study brings to the fore two important issues. First, giving children a chance to voice their perceptions of social participation promotes a greater understanding of what is meaningful to them and what factors limit their social access. Second, the clearly identified discrepancies between children's social participation patterns and preferences emphasize the importance of foundational social development during childhood. Findings highlighted the

importance of understanding children's preferences for the number, intensity, and context of social activities to maximize their opportunities for full participation in life.

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**110.114 114** An Investigation of the Cognitive Factors Underlying Reputation Management in Children with and without Autism. E. Cage*[1], G. Bird[2] and E. Pellicano[3], (1)*Institute of Education*, (2)*King's College London*, (3)*Centre for Research in Autism & Education, Institute of Education*

Background:

Adults often change their behaviour when others are around to manage what people think of them, that is, their reputation. There is currently mixed evidence as to whether children with autism can manage – or think about – their reputation, with the few existing studies suggest that there is much variation in this ability. Understanding the source of this variability is of theoretical and practical import. Potential sources include theory of mind, executive function, social motivation, and understanding of reciprocity. Yet these factors have not been examined in the context of reputation management either in typical development or in autism.

Objectives:

The current study aimed to (1) investigate reputation management in children with and without autism and (2) elucidate the cognitive processes underlying reputation management in both typical development and autism using an individual differences approach.

Methods:

Sixteen children with autism and 16 typical children, aged between 7 and 14 years, and of similar verbal mental age and gender, participated in this ongoing study. Children took part in two tasks measuring reputation management itself; one task in which they played a dictator game once when alone and once when watched by a peer (implicit reputation task) and another task in which they had the opportunity to protect their reputation (explicit reputation task). They also received a battery of tasks indexing theory of mind, executive function, reciprocity and social motivation.

Results:

There was no significant group difference on the task tapping implicit reputation management, as it appeared that neither group was particularly sensitive to being watched (i.e., showed no observer effect). There was also no group differences on the explicit reputation task, although in this case autistic children were just as likely to want to protect their reputation as typical children. While children with autism had additional difficulties with theory of mind, there were no group differences on our measures of social motivation. Within-group correlational analyses showed that individual differences in reciprocity, IQ and executive function correlated with the effect of being watched for children with autism. For typical children, social reward and executive function variables correlated with this observer effect.

Conclusions:

Both children with and without autism may not be particularly sensitive to reputation when it is implicit in nature. This result could mean that subtle reputation management, so prevalent in typical adults, is a skill with relatively protracted development. Interestingly, both groups were keen to protect their reputation when it was explicit that their reputation was at risk. This finding supports previous research that demonstrates that children with autism can present themselves in a certain light when asked to do so. Our findings also suggest that there may be different factors relating to reputation management in typical and autistic children, which may explain some of the variability found in the tendency to manage reputation.

**110.115 115** Association of Social Skill Deficits and Autism Symptomology in Boys with Fragile x Syndrome. D. L. Reisinger*[1], J. Klusek[1], J. Scherr[1] and J. E. Roberts[2], (1)*University of South Carolina*, (2)*Barnwell College*

Background: Boys with fragile X syndrome (FXS) are at high risk for developing autism spectrum disorders (ASD) (Brock & Hatton, 2010). Social

skill deficits are a key symptom of ASD that play an important role in preschoolers' academic, social, and psychological outcomes (Frey, Elliot, & Gresham, 2011; Gillis, Callahan, & Romanczyk, 2011). Social deficits are well documented in FXS, although many studies have not accounted for the impact of ASD comorbidity and it is unclear whether such deficits are characteristic of ASD within the context of FXS rather than of FXS itself.

Objectives: This study compared social skill deficits in preschool boys with only FXS (FXS-O), FXS+ASD, and TD, to examine the impact of ASD comorbidity on the social profiles of children with FXS.

Methods: Participants included boys with FXS-O ($n$=32), FXS+ASD ($n$=21) and typical development (TD; $n$=22) ranging from 36-60 months of age ($M$=46.61, $SD$=6.51). Parent report of children's social skills was obtained using the preschool version of the Social Skills Rating System (SSRS; Gresham & Elliot, 1990). The SSRS is a standardized questionnaire that measures the perceived frequency with which social skills are displayed in the home and the community. The SSRS consists of 4 subscales: Cooperation, Assertion, Responsibility, and Self-Control and a total standard score. The total standard score and the subscale raw scores were used in this study. Autism symptoms were assessed with the Childhood Autism Rating Scale (CARS; Schopler et al., 1988). The CARS consists of 15 items rated on a scale of 1 to 4, with a total score of 30 or above consistent with a diagnosis of ASD; ASD-status of the boys with FXS was determined with the CARS.

Results: A MANOVA indicated a significant effect of group on the SSRS total score ($F$(2,72)=78.65, $p$<0.05)and on all of the subscales: Cooperation ($F$(2,72)=44.389, $p$<0.05), Assertive ($F$(2,72)=40.98, $p$<0.05), Responsibility ($F$(2,72)=32.22, $p$<0.05), and Self-Control ($F$(2,72)=57.38, $p$<0.05). Bonferroni-corrected pairwise comparisons showed that the boys with FXS+ASD had significantly less competent social skills than those with FXS-O ($p$<0.05) across all scores. Both groups with FXS, regardless of ASD-status, displayed less competent social skills than their TD peers ($ps$<0.05) across all scores. The boys with FXS+ASD performed significantly worse than both other groups ($p$<.05) across all scores. The boys with FXS-O also performed worse than the TD boys, but significantly better than the boys with FXS-ASD ($p$<.05).

Conclusions: Findings suggest that social deficits may be an area of concern for those with FXS-O, but even more so for those with FXS+ASD. Furthermore, ASD comorbidity contributes to social skill deficits in young children with FXS but does not account for such deficits entirely.

**110.116 116** Belief Reasoning in ASD: The Role of Language and Executive Functions. C. Irvine*, I. M. Eigsti and J. Mayo, *University of Connecticut*

Background: Deficits in theory of mind are central in autism spectrum disorders (ASD). False belief (FB) tasks are often used to assess theory of mind. Children with ASD show significant delays, not solving FB tasks until age nine (Happé, 1996); typically developing children do so at age four on average (e.g. Wellman et al., 1990). Evidence suggests that language may be a necessary precursor to belief reasoning (e.g. de Villiers, 2005) because "inner speech" provides an on-line representation of another person's perspective. Newton and de Villiers (2007) tested this hypothesis by suppressing inner speech during FB. A non-verbal interference task had no effect, but verbal interference interfered with FB. An alternative explanation suggests that inner speech impacts FB performance via executive functions (EF; Baddeley et al., 2001; Lidstone et al., 2010) including working memory (Hermer-Vazquez et al., 1999). Perhaps language mediates EF via EF's role in belief reasoning (Apperly & Butterfill, 2009). Language deficits are central to ASD; this permits an examination of relationships among language, EF and theory of mind. The present study examines the role of inner speech in FB in ASD. People with autism may rely more heavily on visuo-spatial than linguistic processes (e.g. Williams et al., 2012); verbal loads have a lesser performance impact (e.g. Holland & Low, 2010).

Objectives: Our goals were to test the effects of a) verbal load versus spatial load on FB in ASD and b) verbal load on FB specificity versus EF generality (both false and true belief conditions). We hypothesized that verbal load would disrupt belief reasoning less than visuo-spatial load in ASD, and that load tasks would affect executive functions *generally*, impacting both true and false belief performance.

Methods: Adolescents ages 12-17 with ASD ($n$ = 10; final sample size will be $n$ = 15 per group) and typical development ($n$ = 9) matched on age, NVIQ, and VIQ, $p$'s > .28 viewed silent location change FB and true belief videos, and simultaneously performed verbal load (VL) or a spatial load (SL) task. Participants also completed EF tasks.

Results: Results indicated no main effects of group, belief condition, and no interactions, all p's > .50, with one exception: a significant main effect of load, $p$ = .048, such that performance was worse on VL versus SL across groups and belief conditions. Better VL task performance predicted higher EF scores, p's < .05.

Conclusions: Results of this study suggest that inner speech suppression interferes with belief reasoning equally for individuals with and without ASD, and further, that effects of inner speech suppression are *not* unique to false belief. Verbal load interfered similarly with performance on false *and* true belief tasks. Both false and true belief videos required working memory for complex representations in mind. Findings suggest that inner speech is involved in EF tasks, including belief reasoning, and that individuals with worse baseline EF may be particularly susceptible to effects of inner speech suppression.

**110.117 117** Contribution of Executive Function to Adaptive Behavior Changes over Time. C. E. Pugliese*[1], G. Wallace[2], L. G. Anthony[1], K. M. Dudley[1], A. C. Armour[1] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*NIMH Intramural Research Program*

Background: The development of daily living skills, or adaptive behavior, is particularly challenging for children with ASD. Klin et al. (2007) reported substantially lower adaptive ability compared to cognitive ability in children with high-functioning autism spectrum disorder (HFASD). Specifically, adaptive behavior (social and communication skills) showed a marked decrease with age when examined in a cross sectional manner (Klin et al., 2007). However, conclusions regarding age trends need further study using longitudinal designs. Additionally, it is unclear what factors drive change in adaptive behavior over time. Prior research has demonstrated a relationship between executive functioning and adaptive behavior, such that impairments in executive abilities are strongly associated with deficits in communication, play and social relationships found in children with autism (Gilotty et al., 2002). However, longitudinal research has not confirmed this finding.

Objectives: We sought to determine whether children with HFASD demonstrate longitudinal change in adaptive behavior, and whether baseline executive function predicted such change.

Methods: Participants consisted of 46 children with HFASD (38 male) evaluated through a hospital-based neuropsychology service on two occasions separated by at least six months ($M$=3.24 years, $SD$=1.46 years). Complete data on the Vineland Adaptive Behavior Scales (VABS) and Behavior Rating Inventory of Executive Function (BRIEF) were available at both time points. Participants ranged in age from 3 to 16 years at the first assessment ($M$=8.41, $SD$=2.83), and received a score of at least 70 on either verbal or performance IQ (full scale IQ $M$=102.08, $SD$=21.54). Reliable change indices (RCI) were calculated for composite and domain scores on the VABS for each participant. Clinically significant improvement or deterioration was based on the 95% confidence interval. A multiple regression analysis was conducted to determine whether global executive functioning at time 1, measured by the BRIEF, predicted change in adaptive behavior after accounting for baseline adaptive behavior and full scale IQ.

Results: RCI results indicated 11 participants improved, 7 participants deteriorated, and 23 participants did not change in their standard scores. When participants were divided into two groups based on RCI improvement, no significant differences were found between participants who improved and those who did not improve in regards to age, gender, IQ, or executive function. However, results from the regression model indicated time one VABS Composite score (ß=-0.80, $t$(34)= -4.86, $p$<.001), time one BRIEF global score (ß= -0.33, $t$(34)=-2.05, $p$<.05), and full scale IQ score (ß=0.36, $t$(34)=2.65, $p$<.05) explained 42.2 percent of the variance in the VABS Composite change score ($F$(3,34)=8.26, $p$<.001).

Conclusions: In the first longitudinal investigation of adaptive functioning in children with HFASD, we found that approximately one quarter of the

participants demonstrated growth in standardized VABS scores over time and that executive function abilities, intelligence, and baseline adaptive skill level were all predictive of positive change. These findings have implications for the importance of targeting adaptive skills, and executive functions that contribute to them, in children with HFASD.D.

**110.118 118** Does Greater Social Cognition Lead to More Social Anxiety? Effects of Cognitive Level, Symptom Severity, and Self-Reports of Loneliness on Social Behavior in Adolescents with ASD. A. Pearl, M. Murray*, K. Durica, L. Milliken and A. Heintzelman, *Penn State Hershey*

**Background:** Autism Spectrum Disorder (ASD) is a persistent and debilitating condition accompanied by comorbid disorders. Problems with comorbid psychopathology are prevalent in individuals with ASD, specifically anxiety (While et al., 2009). High-functioning children with ASD have higher levels of anxiety than typically developing individuals (American Psychiatric Association, 2013). Previous research found children with ASD who self-reported high levels of anxiety reported experiencing more loneliness (White & Roberson-Nay, 2009).

**Objectives:** This study examined associations between intelligence, level of impairment, and symptoms of anxiety. Additionally, associations between observed behaviors (e.g., silence, questions asked) and parent- and self-report of symptoms were examined.

**Methods:** Thirty-seven adolescents with ASD (78% male; 97% Caucasian) between the ages of 13- and 18-years-old ($M$=14.57, SD=1.37) were enrolled in a social skills intervention. Adolescents were assessed for verbal intelligence using the Kaufman Brief Intelligence Test, Second Edition (KBIT 2; $M$=104.03, SD=19.68). Parent-report of social impairment (Social Responsiveness Scale; SRS), adolescent-report of loneliness (Loneliness Questionnaire), and parent- and adolescent-report of psychopathology symptoms (Strengths and Difficulties Questionnaire; SDQ) were collected prior to the start of the intervention. Additionally, five-minute conversations between the participants and a same-age peer were collected prior to the intervention and were coded for seconds of silence and number of questions asked.

**Results:** If a participant had a verbal intelligence equal to or below 92, higher SRS scores associated with less seconds of silence. Specifically, higher scores on social cognition (r= -.68, $p$< .05), social communication (r= -.65, $p$< .05), autistic mannerisms (r= -.78, $p$< .01), and the total SRS score (r= -.81, $p$< .01) were associated with less seconds of silence. Additionally, a higher parental report of overall psychopathology associated with less seconds of silence during the behavioral observation (r= -.60, $p$< .05).

If a participant had a verbal intelligence in the average range (i.e., standard score between 93 and 112), higher SRS scores associated with less seconds of silence. Specifically, higher scores on social communication (r= -.63, $p$< .05), social motivation (r= -.66, $p$< .01), and the total SRS score (r= -.72, $p$< .01) were associated with less seconds of silence.

Finally, if a participant had a verbal IQ in the high average range (i.e., standard score above 112), higher social motivation scores on the SRS associated with more seconds of silence (r= .62, $p$< .01). Additionally, for this group higher self-reported loneliness was associated with asking less questions (r= -.67, $p$< .01). Finally, higher parent-reported anxiety (r= .75, $p$< .01) and overall psychopathology (r= .84, $p$< .01) associated with more second of silence.

**Conclusions:** Anxiety is highly comorbid with ASD. Cognitive level and ASD symptom severity may influence the presentation of anxiety symptoms. In this sample, those with the highest IQ's displayed the most overt signs of anxiety (silence during a social conversation) perhaps reflecting greater levels of insight into their challenges. Those with lower IQ's and greater ASD symptom severity demonstrated less overt symptoms of anxiety. This might reflect less self-awareness or less ability to regulate their behavior while anxious.

**110.119 119** Examining the Causal Mechanisms of Positively-Biased Self-Perceptions in Adolescents with Autism Spectrum Disorders. R. Furlano*, E. A. Kelley, L. Hall and D. E. Wilson, *Queen's University*

**Background**: Research has demonstrated that, despite problems in multiple domains, children with Autism Spectrum Disorders (ASD) show a lack of awareness of their difficulties. Previous research on the self-perceptions of children with ASD has focused primarily on examining perceptions of their autism-related traits by

utilizing discrepancy analyses on broad, abstract measures. This method involves difference scores that are calculated by subtracting a criterion score (e.g., parent report) from the child's self-report of competence. The present study aimed to overcome these potential biases by examining the self-perceptions of adolescents with ASD using concrete, familiar, and objective criteria to assess their understanding of academic capabilities.

**Objectives:** To extend research on self-perceptions held by adolescents with ASD. By investigating the relationships between IQ and self-perceptions and executive functioning and self-perceptions, the study hoped to provide a preliminary examination of the underlying causal mechanisms related to biased self-perceptions.

**Methods:** Forty-one participants, 19 with ASD and 22 typically-developing (TD) adolescents (age range =12-18 years), participated. ASD and TD groups were matched on mental age. Self-report questions were utilized after participants completed both verbal and mathematic tasks. Participants were asked how well they thought they did prior to completing the tasks (pre-task prediction). After they completed each task they were asked how well they thought they did (immediate post-performance) and how well they thought they would do in the future (hypothetical future post-performance) Difference scores between actual performance and predicted performance were analyzed. The Delis-Kaplan Executive Function System (D-KEFS) was used as a measure of executive functioning and the Wechsler Abbreviated Scale of Intelligence (WASI) was used as a measure of IQ.

**Results:** A one-way MANOVA was conducted to determine the effect of group diagnosis on the three dependent variables: pre-task prediction, immediate post-performance, and hypothetical future post-performance. Significant differences were found between groups on the dependent measures, Wilks's $\Lambda = .51$, $F(3,37) = 11.70$, $p < .001$, $\eta^2 = .49$. Pairwise comparisons indicated that the ASD group had higher difference scores in pre-task prediction, immediate post-performance, and hypothetical future post-performance questions. Correlation coefficients among difference scores suggest that participants with higher IQ have a more accurate pre-task prediction. Correlation coefficients among difference scores and the D-KEFS suggest that participants with greater abilities in concept formation tend to have a more accurate pre-task prediction while participants with greater abilities in inhibition and cognitive flexibility tend to have more accurate immediate and hypothetical future post-performance self-perceptions.

**Conclusions:** Examining self-perceptions in ASD, using pre/post task self-competence questions, furthers our understanding of the causal mechanisms underlying this phenomenon. It is essential to understand more about the self-perceptions held by individuals with ASD, as a lack of awareness of poor competence may make it difficult for individuals to adjust their behaviour in accordance with feedback This lack of awareness may also limit their ability to incorporate feedback into an understanding of their functioning, thus leading to greater impairment over time. This study may help future research to develop strategies to deal with the potential negative implications associated with overly positive biases.

**110.120 120** Effects of Autistic Traits on Emotion Regulation and Cardiac Vagal Control in Neurotypical Adults. A. Costa* and G. Steffgen, *University of Luxembourg*

Background: Individuals with Autism Spectrum Disorder (ASD) seem to have lower emotion regulation competence (Samson, Huber, & Gross, 2012). It has been reported that ASD is a *continuum* of social-communication disability (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) and that neurotypical individuals are also part of that *continuum* and have autistic traits. Therefore, neurotypical individuals with more autistic traits would be expected to have lower emotion regulation competence than those with less autistic traits. Additionally, low levels of resting heart rate variability (HRV) have been associated with poor social functioning and emotional rigidity (Butler, Wilhelm, & Gross, 2006), which characterize ASD. Consequently, it is hypothesized that neurotypical individuals with more autistic traits should also have lower resting HRV.

Objectives: To analyse if neurotypical adults with more autistic traits use less efficient emotion regulation strategies and the relation to cardiac vagal control.

Methods: 80 undergraduate students participated in the study. None of the participants had a

diagnosis of ASD. Participants were requested to answer four questionnaires: the Autism-Spectrum Quotient (AQ; Baron-Cohen et al., 2001), which comprises 50 items and assesses 5 autistic traits in the general population; the Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004), which comprises 36 items and assesses 6 factors of emotional dysregulation; the Emotion Regulation Questionnaire (ERQ; Gross & John, 2003), which comprises 10 items and assesses 2 emotion regulation strategies, cognitive reappraisal and expressive suppression; and finally, the 20-item Toronto Alexithymia Scale (TAS-20; Bagby, Parker, & Taylor, 1994), which comprises 20 items and assesses 3 factors of alexithymia. In the end, participants' HRV was measured for 5 minutes.

Results: Data collection is still being carried out and therefore definite results cannot be drawn. However, preliminary results seem to indicate that participants who have more autistic traits have in general more difficulties regulating their emotions. They use more often suppression than reappraisal as emotion regulation strategy and demonstrate more difficulties in two factors of the DERS ("Lack of emotional awareness" and "Lack of emotional clarity"). Results also seem to indicate that those with more autistic traits have a higher score in alexithymia. Concerning HRV, preliminary results indicate that those with more autistic traits have higher resting HRV.

Conclusions: Preliminary results indicate that, neurotypical individuals who have more autistic traits have a less adaptive emotion regulation profile compared to neurotypical individuals with less autistic traits. They use more frequently expressive suppression and less frequently cognitive reappraisal and have more difficulties understanding and being aware of their emotions. This could be explained by the fact that, similarly to individuals with ASD, neurotypical individuals with more autistic traits have more difficulties taking another person mental perspective. This is also supported by findings that those with more autistic traits have a higher score in alexithymia, showing that they have more difficulties identifying and describing emotions. The unexpected HRV result might be explained by differences in the pattern of physiological responding (Zahn, Rumsey, & Kammen, 1987).

**110.121 121** Effects of Joint Interaction on Pretend Play Abilities in Children with Prader-Willi Syndrome & Autism Spectrum Disorder. O. Zyga*, S. Russ and A. Dimitropoulos, *Case Western Reserve University*

Background: The processes involved in pretend play are associated with positive skill development in children. Due to its importance, play deficits have been described in children with developmental disorders, including autism spectrum disorder (ASD). It is well established that children with ASD partake in rigid and stereotyped behaviors, which limit their symbolic play abilities. Current research also suggests that individuals with Prader-Willi Syndrome (PWS) have social deficits and repetitive behaviors similar to that of ASD. This link to ASD may result from the genetic underpinnings of PWS. Specifically, PWS is primarily caused by paternal deletions (DEL) of chromosome 15 (q11-13 region), where there is an absence of gene expression from the paternally inherited copy of chromosome 15 or maternal uniparental disomy (mUPD), where two copies of chromosome 15 are derived from the mother. Those with mUPD are at greater risk for ASD symptomatology and duplications of this same 15q11-13 region are strongly associated with autism, occurring in 3-5% of cases with idiopathic autism.

Objectives: The present study sought to further characterize the PWS social phenotype by examining play, and add to current ASD literature on the effects of joint interaction during play. We aimed to identify abilities of pretend play that may be impaired in these populations and determine if the addition of a play partner would increase play abilities in either population.

Methods: 14 children with PWS (mean age = 10.27) and 10 children with ASD (mean age = 10.39), matched for age and IQ, underwent intelligence testing (WISC-IV) and the Autism Diagnostic Observation Schedule (ADOS) as part of a larger, ongoing research project. The ADOS sessions were recorded and play abilities were assessed through a modified Affect in Play Scale (APS; Russ, 2004). Specifically, the modified APS scored participants on scaled measures of comfort, imagination in play, organization of storyline, affective expression in play, frequency of symbolic, functional, and no play acts, and number of repetitive actions during both individual and joint play periods. Measures of

intervention and responsiveness were also scored during joint play to assess if the child's play ability benefited from the presence of an adult, who could scaffold the play for the child.

Results: Preliminary results show that both groups scored at least one standard deviation below normative scores on measure of imagination (ASD = 1.2; PWS = 1.15), organization (ASD = 1.2; PWS = 1.15), and affective frequency (ASD = 0.60; PWS = 0.46) during the individual play period. Results also indicate that the addition of a play partner during the joint play period increased all scaled scores on the APS. Within the ASD group, joint interaction increased the frequency of symbolic play. However, for the PWS group, joint play led to a frequency increase in all types of play.

Conclusions: These results suggest that structured interventions targeting specific pretend play abilities (i.e. symbolic play, organization, and affect) for children with ASD and PWS may help increase this skill set and may help social and emotional development within these populations.

**110.122 122** Evaluating the Social Abilities of Children with Autism Spectrum Disorders and Complex Communication Needs. M. Murray*, A. Pearl, L. Milliken and K. Durica, *Penn State Hershey*

**Background:** It has been well recognized that non-verbal children with Autism Spectrum Disorders (ASD) are underrepresented in the research literature, especially when considering social interaction abilities. Recently, an expert panel convened by NIH highlighted the need for research in this population and recommended the development of creative solutions for assessment of non-verbal school-aged children with ASD that could be used for descriptive information and to measure outcomes for research participants. Domains recommended for consideration included joint attention skills and social impairment severity.

**Objectives:** To measure these outcomes systematically, an assessment battery was created which includes the Social Responsiveness Scale (SRS) and a novel behavior assessment, the Standardized Joint Attention Assessment (SJAA), which measures initiation of joint attention (IJA) abilities. The SJAA was designed to measure IJA bids that are made by participants purely for social engagement. Participants who are viewed as being more socially capable by their teachers and caregivers should evidence higher rates and more complex IJA bids during the SJAA.

**Methods:** Eleven non-verbal (defined as fewer than 10 functional words) children with ASD between the ages of 8 and 15 were enrolled in this study. Parents and teachers of the participants completed the SRS. The participants received the SJAA, which includes a series of 15 second clips from highly preferred videos activated at regular intervals from different sources. This provides opportunities for the child to initiate the sharing of his or her attention with a confederate social partner. The confederate social partner does not reference the stimulus unless the participant makes an IJA bid and modifies their response to the participant such that there is opportunity for 2 potential IJA bids per clip.

Each participant's SJAA was videotaped; the complexity of IJA bids was coded on a 4 point scale. Each participant received a first bid and a second bid score which is created by summing the complexity coding of any first bids and any second bids offered. This number is divided by 16, the total number of possible clips, creating IJA proficiency rates.

**Results:** Factors of interest for data analysis included SRS scores and IJA proficiency rates. The teacher-report total SRS score negatively correlated for first bid scores ($r=-.64$, $p<.05$) and second bid scores ($r=-.65$, $p<.05$). Additionally there were negative correlations between second bid scores and the social awareness ($r=-.68$, $p<.05$) and social motivation ($r=-.61$, $p<.05$) subscales of the SRS. The parent-report SRS scores did not correlate with SJAA scores.

**Conclusions:** The SJAA offers a systematic means of measuring IJA proficiency in non-verbal school-aged children with ASD. This assessment is novel in that any offered IJA bids by participants are for engagement with a social partner and not dependent on expressive language abilities. The scoring algorithm quantifies social proficiency in a clinical population that is difficult to characterize and is in dire need of assessment strategies with clinical relevance. SJAA bid scores negatively correlating with teacher-report SRS scores but not with parent-report SRS scores points to the

difficulty of assessing social capabilities in this population.

**110.123 123** Examining the Relationship Between Birth Order and Birth Interval and the Emotional and Behavioral Adjustment of Siblings of Children with Autism. K. Campe*[1], F. I. Jackson[1], E. Hanson[1] and A. V. Snow[2], (1)*Boston Children's Hospital*, (2)*Boston Children's Hospital, Harvard Medical School*

Background: Sibling relationships are known to have a significant impact on children's social and emotional development (Dunn, 1988). Studies have focused on the adjustment of typically developing (TD) siblings of children who have an autism spectrum disorder (ASD) have had mixed results; some showing positive effects for TD siblings (Macks et al., 2007), others demonstrating negative effects (Dempsey, 2012). Several variables appear to moderate the effect of having a sibling with ASD (Campe et al., 2013). Previous studies have examined the impact of birth order (Warren et al., 2012), yet the impact of birth interval has received little research attention in the ASD population (Martin & Horriat, 2012). Such studies have suggested that TD siblings who are younger and closer in age to their sibling with ASD tend to have more difficulties. However, these studies have been limited by small samples.

Objectives: This study sought to examine how birth order and birth interval impact the emotional and behavioral adjustment of TD siblings of children with ASD using a large heterogeneous sample, within group comparisons, and non-parametric statistics.

Methods: A sample of 926 children with ASD and their TD siblings (463 sibling pairs) were drawn from the Boston cohort of the Simons Simplex Collection and the Boston Autism Consortium. Participants were between the ages of 25-216 months (mean=105, SD=46). 232 TD siblings were older than their sibling with ASD, 319 TD siblings were younger, and there were 12 sets of twins (TD+ASD) with in the sample. The Child Behavior Checklist (CBCL) was completed for all TD siblings. For birth interval analyses, TD siblings were classified into groups based on the difference in age from their sibling with ASD, in 24-month intervals (i.e. 48-72 months younger, 24-48 months younger, <24 months younger, twin, <24 months older, 24-48 months older, 48-72 months older). Non-parametric statistics including Kruskal-Wallis tests with Mann-Whitney comparisons were conducted to examine the impact of birth order and birth interval on the behavior profiles of TD siblings as measured by the Child Behavior Checklist.

Results: Analyses revealed a trend of higher rates of externalizing problems in younger TD siblings of children with ASD ($p<.1$) which is commensurate with findings from previous research. Birth interval analyses revealed that high rates of externalizing symptoms were consistent across birth intervals in younger siblings of children with ASD. Among older siblings, those who were 24-48 months older had the lowest rates of externalizing behaviors, including significantly lower rates of aggression. Analyses of Internalizing symptoms indicated similar rates in younger versus older TD siblings. Among the older TD siblings, however, those who were 48-72 months older had significantly higher rates of anxious/depressed symptoms.

Conclusions: Consistent with previous research, younger siblings of children with ASD appear to have a higher rate of behavioral difficulties overall. Protective and deleterious effects of birth interval were found for older siblings of children with ASD only.

**110.124 124** Eye Tracking Utilizing Age Matched Social Scenes and Geometric Shapes. K. Gaietto*[1], R. Shaffer[2], K. Warner[3], L. Mathieu-Frasier[2], C. Erickson[2] and L. K. Wink[2], (1)*University of Cincinnati*, (2)*Cincinnati Children's Hospital Medical Center*, (3)*University of Kansas Medical Center*

**Background:** Social impairment is a key characteristic of patients with Autism Spectrum Disorders (ASD). In the current search for therapies to improve the symptoms of ASD, it is imperative to have quantitative, objective clinical measures of social deficits in order to evaluate the efficacy of these potential therapies. Eye tracking, a relatively new phenomenon in ASD research, holds promise as a potential measurement tool for evaluation of experimental therapies' efficacy. Previous research has suggested that there is a difference of viewing preferences between toddler social scenes and geometric shapes in individuals with ASD compared to neurotypical (NT) peers.

**Objectives:** Considering that age may impact the saliency of social stimuli, this study aimed to evaluate the viewing preferences of children with ASD and neurotypical peers when given the choice

between age-matched social scenes and geometric scenes.

**Methods:** Eye tracking data was collected for both the ASD and NT participants. Social Communication Questionnaire (SCQ) score was collected for both groups, and Intelligence Quotient (IQ), Social Responsiveness Scale (SRS), Aberrant Behavior Checklist (ABC), and Vineland scores were collected for the ASD children. The study participants included children ages 6-11 and the eye tracking paradigms presented school-aged children. Each subject viewed three eye tracking paradigms, which were each presented next to a video of moving geometric shapes. The videos were randomly assigned to right versus left to control for a side bias. Total fixation duration of the social scenes and total fixation duration of the geometric scenes were recorded and the ratio of preference was calculated. The preference ratio was compared between the ASD and NT groups.

**Results**: The final sample consisted of 28 participants with ASD and 18 neurotypical peers. There were 37% female and 63% male in the study. Total viewing time of the social scenes significantly differed between the two groups ($t = -3.726$, $p = 0.001$), while geometric viewing was not significantly different ($t = 1.199$, $p > 0.05$). When the ratio between the two types of scenes was compare, a significant difference was found between the ASD and NT groups in their viewing preference ($t = -2.534$; $p < .05$). The ASD group demonstrated decreased preference for viewing the social scenes relative to their NT peers. This relationship was mediated by SCQ score. As SCQ score increased, there was a decreased preference for viewing the social scenes. The other testing variables collected did not have a significant impact on the difference between the two groups.

**Conclusions:** This study found that when social stimuli presented is age-matched, children with ASD still demonstrate a decreased preference for social scenes relative to their NT peers. These findings are similar to the results from a comparable study in which children viewed toddler social scenes versus geometric shapes. Further studies should be conducted to determine if other metrics mediate viewing preferences as SCQ did. Once a better understanding of the social versus geometric scene preference in ASD is established, eye tracking could be a useful tool to evaluate the effectiveness of novel ASD therapies.

**110.125 125** Eye-Gaze Patterns during Live Social Interactions in Children with Autism Spectrum Disorders. M. W. Gower, S. A. Koch*, H. D. Johnson, M. I. Hopkins, F. R. Amthor and F. J. Biasini, *University of Alabama at Birmingham*

Background: Children with autism have been shown to demonstrate deficits in their face processing skills and to make less eye contact than typically developing peers. It has also been assumed that children with autism are more anxious during social interactions than typically developing children. It has been suggested that these deficits manifest themselves through a localized facial processing style in which children with autism focus on the lower face and miss much of the pertinent social information conveyed by the eyes. More recent research has found contradictory evidence. Studies have shown that children with autism look at the eyes as often as their peers when viewing happy faces; that the eye-to-mouth gaze ratio is the same as that of typically developing children, but those with autism tend to focus more on non-social background stimuli; and that children with autism are not more anxious during social situations than typical children.

Objectives: This study utilized eye-tracking technology, real-time physiological measurements, and live social interactions to compare eye-gaze patterns and physiological reactions between children with autism and typically developing children.

Methods: 13 children ranging from 8- to 14-years-old completed this study. Approximately half of these children had diagnoses of autism spectrum disorder (n=6), while the other half were typically developing (n=7). All participants took part in two separate interaction sessions with their caregiver and an unfamiliar adult. The durations of the interactions ranged from four to seven minutes, with most interactions lasting five minutes. While each of these interactions took place, faceLAB™ eye-tracking technology was used to monitor eye-gaze patterns of the participants. Concurrently, LifeShirt® technology measured physiological changes in participants indicative of anxiety (heart rate, respiration rate).

Results: When compared to typically developing peers, children with autism tended to exhibit very similar total percentages of interaction time fixated on the eyes, $F(1,10)=2.61$, $p=0.137$, mouth, $F(1,10)=2.48$, $p=0.147$, and non-face

areas, $F(1,10)=0.58$, $p=0.464$. However children with autism exhibited significantly shorter look durations to the eyes when compared to their peers, $z=-1.786$, $p=.037$. Furthermore, children with autism did not exhibit different levels of anxiety during either familiar or unfamiliar interactions, as measured by heart rate while talking, $F(1,10)=0.49$, $p=0.499$, and while not talking, $F(1,10)=0.70$, $p=0.423$), as well as respiration rate while talking, $F(1,10)=0.08$, $p=0.781$, and while not talking, $F(1,10)=0.10$, $p=0.757$.

Conclusions: Children with autism tend to look at the eyes, mouth, and non-face regions for similar total amounts of time as typically developing children. However, children with autism exhibit significantly shorter look durations to the eyes than their peers, especially when speaking to a familiar individual. These findings suggest that the difficulty children with autism experience in understanding social information may be due to constantly switching their attention to and from the eyes, rather than focusing and processing the social cues that the eyes convey. Finally, these results suggest that children with autism do not exhibit any greater anxiety than typically developing children during familiar or unfamiliar social interactions.

**110.126 126** Friendship and Depression Among Children with ASD. J. Mendelson*[1], S. P. Keane[2], R. Nelson-Gray[2] and M. D. Lerner[3], (1)*University of North Carolina - Greensboro*, (2)*UNC-Greensboro*, (3)*Stony Brook University*

Background: Friendship quality and quantity is associated with a range of positive functions among typically developing children. These included, but are not limited to: buffering against depression and anxiety (e.g., Bukowski, Laursen, & Hoza, 2010) and fostering self-esteem and school achievement (e.g. Hartup, 1996; Newman-Kingery, Erdley, & Marshall, 2011). However, children with Autism Spectrum Disorders (ASD) struggle to form reciprocal friendships , and have been found to describe their friendships differently than do typically developing children (e.g. Bauminger & Kasari, 2000; Carrington et al., 2003; Marks et al., 2000). To date, only one study has examined the relation between participation in a reciprocal friendship and commonly associated outcomes among individuals with ASD (Mazurek & Kanne, 2010), with findings unexpectedly suggesting that individuals with ASD and at least one friendship are at elevated risk for anxiety. However, no investigation has yet examined the relationship of depression to friendship *quality* in this population.

Objectives: To examine associations between friendship quality (Friendship Quality Questionnaire; FQQ; Parker & Asher, 1993), with depression (Child Depression Inventory; CDI; Kovacs, 2004). It was hypothesized that, as in typically-developing populations, higher quality friendships overall would predict lower levels of depression.

Methods: The FQQ and the CDI were administered to 30 boys aged 8-16 (mean=12) who presented for a screening prior to participation in a social skills based day camp for children with ASD. All participants were reported to have received a diagnosis of ASD through a community provider, and diagnosis was confirmed using the Gilliam Asperger's Disorder Scale (Gilliam, 2001). The FQQ consists of 6 subscales measuring positive and negative aspects of friendship.

Results: FQQ total scores correlated positively with CDI scores ($r = .39$, $p = .035$) This relation was driven by the Conflict and Betrayal ($r = .46$, $p = .011$) and Intimate Exchange ($r = .43$, $p = .017$).

Conclusions: Contrary to hypotheses, friendship quality predicted higher depression, with the Conflict and Betrayal and Intimate Exchange subscales driving the relation. Findings suggest that conflict and betrayal and intimate exchange in friendships may actually predict depression among children with ASD. This suggests that, while friendship has been found to serve an important buffering role among typically-developing children primarily through its function as a source of positive affective exchange (e.g., Newcomb & Bagwell, 1995), this role may be different for children with ASD, who struggle to comprehend affective cues. However, difficulty describing internal states has traditionally been associated with a diagnosis of ASD (e.g., Bauminger & Kasari, 2000). Because children with ASD may not be as perceptive of positive affective cues, findings suggest that those who were more adept at describing their feelings may also be more sensitive to negative cues from the social environment (which may be delivered more concretely, such as in the form of bullying). Thus, findings may actually relate to a third variable of ability to describe one's own inner state, such that

children who were better able to describe their friendships were also better able to describe feelings of depression.

**110.127 127** Group Social Skills Intervention for High-Functioning Children with Autism Spectrum Disorder: Process and Outcomes. J. K. Goodlad, T. S. Tomeny, E. C. Fair* and T. D. Barry, *The University of Southern Mississippi*

Background: Given that social impairment is a key feature of autism spectrum disorder (ASD), social skills training remains paramount. The present eight-session intervention, led by two Masters level clinicians, was designed to address a variety of deficits reported by parents: friendship management, staying on topic, taking turns and other conversational skills, recognizing feelings, keeping calm, and hygiene. After completing an initial assessment, adolescents with ASD and an estimated IQ in the average range or above were admitted. Group participants were Caucasian males aged 12 to 17 (M = 14) with Gilliam Asperger's Disorder Scale (GADS) quotients ranging from 100 to 127 (*M* = 111.8, *SD* = 10.57) and Autism Spectrum Symptom Questionnaire (ASSQ) scores ranging from 24 to 42 (*M* = 33.6, *SD* = 7.16) Five typically-developing peers from local high schools also attended the group as social models.

Objectives: The current study aimed to describe and examine an outpatient clinic-based social skills group intervention with five high-functioning adolescents with ASD.

Methods: Each session included 5 general components: a warm-up activity to promote group interaction; an instructional component to teach new skills; snack time to promote unstructured practice of new skills; guided role-play and active practice of new skills; a review of skills discussed and conclusion; and the assignment of homework to facilitate practice of skills outside of the group. Parents were provided a review of each session, including the skills covered and the assigned homework. During each two hour session, adolescents received approximately 1.5 hours of direct skills training and active structured practice; the remaining 30 minutes (e.g., snack, assessment) allowed opportunities for spontaneous practice of skills. Each week's session focused on a new social skill, including getting to know others and starting a conversation, turn-taking in conversation and activities, self-monitoring of appropriate and inappropriate comments, perspective-taking, nonverbal communication and intentions behind comments, understanding emotions in self and others, and social problem solving. Adolescents with ASD were assessed before the group and at the last meeting using self- and parent-report measures, including the Behavioral Assessment Schedule for Children (BASC-2), Autism Spectrum Screening Questionnaire (ASSQ), Gilliam Asperger's Disorder Scale (GADS), and the Social Skills Rating System (SSRS). Adolescents and group leaders completed the Therapeutic Alliance Scale for Children (TASC-R).

Results: Mean scores on BASC-2 subscales at pre- and post-group showed a slight trend in improvement in many areas across time. Though modest, these changes were observed after only 8 weeks of treatment despite the test-retest reliability of the BASC-2. a strong negative correlation, although only a statistical trend, was observed between group leader ratings on the TASC-R and ASSQ scores ($r$ = -.92, $p$ = .08).

Conclusions: Overall, these results suggest improvements following group inclusion, and with extended treatment, effects may be even stronger. Though clinicians should be cognizant of their own viewpoints and biases with this population, even with treatment gains.

**110.128 128** Intellectual and Social Cognitive Functioning in Monozygotic and Dizygotic Twins with ASD. N. T. Bott*, J. Phillips, J. F. Hallmayer, S. Cleveland and A. Y. Hardan, *Stanford University School of Medicine*

Background: Autism is a highly heritable neurodevelopmental disorder. Previous studies have found sub-threshold social impairments in siblings of children with ASD, as well as in unaffected twins.

Objectives: The primary aim of this investigation was to examine the intellectual and social cognitive functioning of monozygotic and dizygotic twins with ASD, with at least one affected twin. This was part of a larger study examining the behavioral and neural correlates of twins with ASD, their siblings, and neurotypical twin pairs.

Methods: Monozygotic and dizygotic same-sex twins with ASD, and age-, gender- matched neurotypical twins between the ages of 6 and 14 years were included. Intellectual functioning was assessed using the Stanford-Binet Intelligence

Scales (SB5). Social abilities were assessed using the Social Responsiveness Scale (SRS), the Theory of Mind (ToM) and Affect Recognition (AR) Social Perception subtests of the NEPSY-II, as well as a reading the mind in the eyes (Eyes) task, and a Theory of Mind (Smarties) task.

Results: A total of 92 participants were included in this investigation: 24 monozygotic with ASD, 40 dizygotic, and 28 neurotypical twins (12 MZ, and 16 DZ). There was no significant difference in age or gender between groups. Difference scores (Δ= Most severe – least affected) on intellectual and social cognitive measures were compared between MZ and DZ neurotypical pairs. As expected, a significant difference was found on the Δ score between monozygotic and dizygotic ASD twin pairs on the SRS total T-score with a trend toward significance on FSIQ score. When comparing the most severe proband between monozygotic and dizygotic twins, there were no significant differences on intellectual abilities or social cognitive functioning measures. The least severely affected MZ probands performed significantly better than the most severely affected DZ probands on both affect recognition tasks (AR and Eyes).

Conclusions: Findings from this study suggest that the most severe probands of MZ and DZ twin pairs do not differ significantly from one another on several clinical measures. Interestingly, the least severely affected MZ probands perform better on measures of affect recognition than the most severely affected DZ probands, raising the question of whether aspects of affect recognition are less heritable. This observation is intriguing, but final conclusions cannot be made in light of the small sample size. These preliminary findings warrant additional investigation to comprehensively examine all aspects of intellectual and social cognition in monozygotic and dizygotic twins with autism of all ages.

**110.129 129** Measuring Contextualized Social Attention Using Eyetracking: A Promising Behavioral Biomarker of Autism Spectrum Disorders. C. Chevallier*[1], J. Parish-Morris[2], A. McVey[1], K. Rump[1], J. Herrington[2] and R. T. Schultz[2], (1)*Center for Autism Research, The Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*

**Background:** In the past decade, a number of studies have used eye tracking technology to quantify attention to social scenes. Taken together, these studies converge to demonstrate that individuals with ASD display increased attention to background objects and decreased attention to faces and people compared to controls (e.g., Bradshaw, Shic, & Chawarska, 2011; Klin, Jones, Schultz, Volkmar, & Cohen, 2002). More recently, research has focused on clarifying the mechanisms behind such diminished attention to the social world by examining how context impacts visual atypicalities in ASD.

**Objectives:** In this study, we extended this work by investigating the robustness of contextualized social attention as a behavioral biomarker of ASD in a large sample of children spanning all levels of functioning and a wide range of ages.

**Methods:** 162 children (*N* ASD = 106) were included in the study to examine the relationship between eyegaze patterns and phenotypic data. In order to look at group differences, a subset of 38 children with ASD was closely matched on age and IQ to 38 Typically Developing Controls (TDCs). Finally, another subset of 56 kids (*N* ASD = 32) who came at two different time points separated by a 9 week interval was analyzed to examine test-retest reliability. Social context was manipulated by having participants watch videos of children playing either *jointly* or in *parallel*. Eyegaze patterns were collected at a rate of 60 Hz using a Tobii X120 tracker. Total fixation duration to faces or objects relative to the fullscreen was calculated for each participant, and correlated with phenotypic information.

**Results:** Correlations on the entire sample demonstrated that Total Fixation Duration to faces was associated with independent measures of social skills (e.g., SRS, SCQ) but not with cognitive non-social scores (e.g., DAS). Analyses on the matched groups revealed a Diagnosis x Stimulus-Type interaction (due to ASD children looking less at faces than the TDCs) and a strong Context x Diagnosis x Stimulus-Type interaction. This three-way interaction was due to group differences being significant in the joint condition but not in the parallel condition. We then looked at the test-retest reliability of this behavioral index (i.e., TFD to faces in the joint condition) using intraclass correlations and found it to be extremely reliable across our two time points.

**Conclusions:** Our results revealed that 1) time spent looking at faces correlated with independent measures of social skills, 2) Interactive contexts

are best for eliciting group differences, and 3) this behavioral index is stable across time. As such, we suggest that time looking at faces presented in an interactive context might constitute an interesting behavioral biomarker of autism.

**110.130 130** Parent-Child Interaction in Children with Autism Spectrum Disorder and Their Siblings: Comparison of Two Coding Procedures. C. Bontinck*[1], P. Warreyn[1], M. Meirsschaut[2] and H. Roeyers[1], (1)*Ghent University*, (2)*Artevelde Hogeschool*

**Background:** Parent-child interaction strongly influences the emotional, behavioral, and cognitive development of young children. In a supportive, positive parent-child interaction children can learn and practice a range of abilities (e.g. coping, social skills, etc.). However, given the social-communicative deficits associated with ASD, it is often difficult for parents to interact with their child with ASD. Consequently, parent-child interaction has become an essential part of early interventions for young children with ASD. Given the importance of these parent-child interactions, it is crucial that they can be accurately assessed. Nevertheless, there is no consensus as to how these interactions should be coded.

**Objectives:** The aim of the current study was to investigate whether the mother-child interaction in children with ASD differs from the mother-child interaction in their younger siblings. To this end, we compared two coding procedures: a global coding using the rating scales of Erickson and a detailed, more time-consuming procedure (see Meirsschaut et al., 2011).

**Methods:** 16 mothers were observed during a task interaction separately with their child with ASD (M=68 months, range=46-84) and with a younger unaffected sibling (M=48 months, range=29-67). All interactions were videotaped and the 32 videos were coded twice. For the global coding mothers were rated on five seven-point scales: supportive presence, respect for the child's autonomy, structure and limit setting, hostility, and quality of instruction. Children were rated on four seven-point scales: non-negativity, non-avoidance, compliance, and affection. Child characteristics (e.g. developmental age, word comprehension, gender, etc. ) were also taken into account. The detailed coding scheme consisted of 2 broad categories: social initiatives (declarative, imperative, or neutral) and social responses (confirming, non-confirming, neutral, and attempt to comply). Both interval coding and frequency coding were applied during three runs of the videos.

**Results:** Using the global coding procedure, we found that mothers scored significantly higher on supportive presence, structure and limit setting and quality of instruction with their children without ASD. The different scales in our global coding scheme did not capture any differences in the children's social behavior. From the detailed coding procedure we could conclude that mothers were more responsive with the non-ASD sibling. Additionally, children with ASD were proportionally more imperative and less declarative.

**Conclusions:** Our main finding is that, contrary to what we expected, mothers were more structuring and supporting with their children without ASD. Methodologically, the global coding scheme detected more differences in the mother's social behavior and seemed better suited for coding interactions and relational or emotional aspects. The detailed coding scheme was better for detecting differences in the children's social behavior. Additionally, this coding procedure was better suited for coding specific abilities and technical aspects of the interaction. In summary, both coding procedures seem to complement each other well.

**110.131 131** Perceptions of Bullying Among Youth with and without Autism Spectrum Disorders. K. A. Scheil*[1] and R. M. Kowalski[2], (1)*University of Kentucky*, (2)*Clemson University*

Background: In the first national study examining bullying in the United States post Columbine, Nansel and her colleagues (2001) found that 17% of middle- and high-school students experience moderate to frequent victimization. Until recently, bullying research has predominantly focused on neurotypical students in general education settings; however, emphasis on individuals with special needs has begun to increase. Previous literature suggests that individuals with autism spectrum disorders (ASDs) are at greater risk for both traditional and cyber bullying victimization and perpetration than their typically developing peers (Little, 2002). Additionally, researchers claim that youth with ASD may struggle to comprehend bullying dynamics due to deficits in their social and communication skills. Specifically, individuals with ASD often display deficits in Theory of Mind, or the "ability to attribute mental

states to themselves and others in order to explain and predict behavior," which may affect their ability to navigate and comprehend social interactions (Colle, Baron- Cohen, & Hill, 2007, p. 716).

Objectives: To date, only one study has investigated *perceptions* of bullying among youth with ASD (Van Roekel et al., 2010). The present study aimed to further develop an understanding of bullying experiences among youth with ASD based on parent and child online surveys and semi-structured interviews.

Methods: Children with and without ASD answered questions related to past traditional and cyber bullying experiences, communication with their parents, perceptions of bullying scenarios, and Internet/cellular phone use and safety. Parents of these youth participants were asked similar questions about their children's experiences. As another measure to assess perceptions of what constitutes bullying, children identified six images (4 bullying, 2 neutral) as either bullying or nonbullying (Saylor et al, 2012).

Results: Prevalence rates of victimization and perpetration were higher among youth with ASD in comparison to their peers without disabilities as reported in both parent and child interviews. Interviews with parents of children with ASD highlighted various deficits in their children's social comprehension skills, and youth with ASD also noted difficulties in understanding bullying dynamics (e.g., incorrectly defining bullying, struggling to understand humor, failing to recognize others' perspectives). Additionally, children with ASD did not perform as well as children without ASD in the ostracism picture identification task. In fact, two-thirds of the children with ASD incorrectly identified at least one of the six bullying/nonbullying scenarios while none of the children without ASD inaccurately labeled a picture.

Conclusions: Without this ability to understand others' behaviors and intentions, youth with ASD may misinterpret bullying dynamics in their everyday lives. These unique deficits in social understanding may explain why several youth with ASD failed to recognize their own experiences of victimization and perpetration. Given that these youth may not possess the necessary skills to comprehend complex bullying dynamics, interventions to increase their social comprehension may help these individuals recognize and report bullying incidences in which they or their peers are involved.

**110.132 132** Performance on a Novel Kinect Emotional Choice Game Correlates with Broader Autism Phenotype Characteristics in Typically Developing Adults. M. Weng*, E. S. Kim, C. A. Wall, M. G. Perlmutter, E. R. Lebowitz and F. Shic, *Yale University School of Medicine*

Background: While video game overuse has caused difficulties in the lives of some individuals with autism spectrum disorders (ASD) (Mazurek et al., 2011), video gameplay may provide a useful way to measure social cognition. We designed a video game that physically engages participants in a fun, unstructured task that implicitly measures emotion processing, using the Microsoft Kinect platform. Difficulties in emotion processing and other autistic-like traits have been shown to vary beyond populations with ASD diagnoses, with ASD representing extrema (Lundstrom et al., 2012).

Objectives: To examine relationships among preferences for emotional information expressed through whole-body, volitional actions, the ability to recognize emotional information, and traits associated with the broader autism phenotype.

Methods: TD adults ($N$ = 19; 5 females; age $M$ = 22.7 years, $SD$ = 6.1 years; FSIQ $M$ = 111, $SD$= 21.85) played a video game on the Kinect platform using the custom-built Yale Interactive Kinect Environment Software (YIKES). Live video images of each participant were integrated in the game environment, which was projected on to a wall. The participants were asked to move left and right to position their images to catch emotional (fearful, happy, and neutral) faces "falling" from the top of the screen. A total of 280 face images were presented,divided over eight rounds of gameplay. Outcome variables were ratios of number of emotional (fearful or happy) faces, to total number of faces caught, in each of round. Given the large number of variables associated with gameplay dynamics and high levels of correlations among variables, we used principal component analysis (PCA) for dimensionality reduction. We examined correlations (Pearson's) between the identified principal components (PCs) and performance on the Developmental Neuropsychological Assessment (NEPSY-II) Affect

Recognition subtask, the Broader Autism Phenotype Questionnaire (BAPQ), and IQ (measured using the Wechsler Abbreviated Scale of Intelligence; WASI).

Results: PCA revealed 3 factors accounting for 83% of all variance: principal component 1 (PC1: 51% of variance) represents diminished selection of negative (fear) content and increased selection of positive (happy) content; PC2 (21%) represents increased selection of any emotional content; and PC3 (11%) represents avoidance of negative content and selection of positive content specifically in mood-negative contexts. PC1 showed no correlations with any examined phenotypic characteristic. PC2 was associated with lower BAPQ scores ($r$ = -.47, $p$ < .05) and with higher Affect Recognition scores ($r$ =.47, $p$ < .05). PC3 correlated with performance IQ ($r$ = .46, $p$< .05).

Conclusions: Performance on a simple, emotional-choice, whole-body-movement video game can provide information about phenotypic characteristics of typical adults. Correlations between PC2 and BAPQ or AR scores suggest that preferential orienting towards emotional information is related to the ability to identify emotions in pictures of faces, and to fewer broader autism features in TD adults. These results provide evidence that video games may be used as an appealing platform for understanding cognitive ability, emotional processing, and social capabilities. Future directions include extension to children and to individuals with ASD, and exploration of therapeutic applications.

**110.133 133** Predicting Empathy: The Interaction Between Indices of Reactivity and Regulation in Autism and Typical Development. J. C. Sullivan*, S. A. Schoen and L. J. Miller, *Sensory Processing Disorder Foundation*

Background: Children with autism spectrum disorders (ASD) are known to display quantitative differences in their processing of sensory stimuli, most often studied at the level of negative sensory reactivity, which are hypothesized to play a role in atypical social behaviors. One often-neglected area of sensory processing, however, is in the regulation of these negative emotions, and how these two components (reactivity and regulation) might interact to affect social behavior.

Objectives: This study aimed to investigate the relationship between one expression of sensory reactivity, sensory over-reactivity (SOR), and a temperamental measure of self-regulation, effortful control (EC), with a measure of parent-reported empathy. How this relationship might differ between typically developing children and children with ASD was additionally explored, as was age-related changes in this association.

Methods: Parents of 100 typically developing children (2-9 years old, 52% male) and 97 children with ASD (3-9 years old, 80% male) completed questionnaires about their child including the Sensory Over-Responsivity Inventory (SOR), the Effortful Control subscale of the Very Short Children's Behaviour Questionnaire (EC), and the Children's Empathy Quotient (EQ). Scores on the Autism Quotient 'red-flags' version were additionally utilized to confirm high autism risk in the ASD group and low risk in the typical group.

Results: Children with ASD were reported to show less EC, more SOR, and lower EQ scores than the typically developing children. In the typical sample, greater EC and lower SOR was associated with higher EQ scores, but there was also an interaction between EC and SOR such that children with a combination of high SOR and high EC scored the highest on the EQ, while high SOR and low EC predicted the lowest EQ scores. There was also an age interaction in the typical sample, such that the the EC/SOR interaction effect on EQ strengthened with age. In the ASD sample, however, the pattern was very different, only EC playing any role in EQ and no age interactions noted.

Conclusions: The relationship between SOR and EC in predicting empathy may be different in ASD than it is in typically developing children. Results are discussed with regards to sensory reactivity, self-regulation, and empathy in the general population as well as possible explanations for a lack of relationship between these variables in ASD.

**110.134 134** Processing of Self-Referential Information in High-Functioning Children with Autism. C. A. Burrows*, L. V. Usher and H. A. Henderson, *University of Miami*

Background: Developing a strong sense of self is an important developmental precursor for understanding others and developing social skills.

Preferentially remembering self-relevant information, particularly of positive valence is an adaptive process, leading to enhanced self-esteem and efficient memory storage and retrieval. In general, it appears that individuals with autism do not efficiently scaffold personally relevant information, as they do not demonstrate the typical pattern of preferentially remembering self-relevant over other-relevant information. This may hinder their ability to understand their thoughts and emotions as well as the experiences of others, leading to the observed social skill deficits. However, little is known regarding the mechanisms underlying these differences in self-representation.

Objectives: The current study seeks to examine the role of the emotional valence (positive and negative) of self-relevant trait adjectives in influencing how individuals with autism process self-referential information.

Methods: Participants with high functioning autism (HFA; N=73, 62 males, $M_{age}$=12.56, SD=2.60) and a matched comparison sample (COM; N=64, 46 males, $M_{age}$=13.56, SD=2.01) completed a self-referenced memory paradigm, where they were asked to judge whether trait adjectives were characteristic of themselves, characteristic of another person, or based on a structural feature of the word. An equal number of positive and negative adjectives were included in each condition. After a short delay participants were asked whether they recognized the adjectives from a list of the original words interspersed among additional novel distractor adjectives.

Results: A repeated-measures ANOVA was conducted to examine the differences in rates of adjective endorsement based on valence and personal relevance. Results revealed a significant Group by Valence interaction in endorsements of self-relevant adjectives, $F(1, 135)= 5.51$, $p$=.02, but not in endorsements of other-relevant adjectives, $F(1,131)=.29$, $p>.05$ . In the self-referential condition, children with HFA (M=2.37, SD=1.72) endorsed greater rates of negative adjectives than their COM peers (M=1.54, SD =1.46), but comparable levels of positive adjective endorsement ($M_{HFA}$=5.42, SD=1.43; $M_{COM}$=5.51, SD=1.20). There were no group differences in rates of endorsement of positive or negative adjectives when children referenced another person. To examine the relationship between endorsement and recognition, a hierarchical linear regression was run, including age and verbal IQ as covariates. In the COM group, the endorsement positivity bias, or difference between number of positive and negative adjectives endorsed, predicted preferential self-referenced memory, over and above the effect of age and verbal IQ, $F(3, 55)=6.17$, $p$=.001, $R^2$=0.25, $R^2_{change}$=0.22. This was not true for the HFA participants, $F(3, 64)=0.24$, $p>.05$, $R^2$=0.01.

Conclusions: As hypothesized, HFA participants demonstrated a reduced positivity bias when compared to their typically developing peers, which was driven by greater rates of endorsement of negative self-relevant adjectives. Interestingly, endorsement rates related to later memory performance in COM but not HFA individuals. The reduced positivity bias in individuals with autism may de-couple the associations between endorsement and recognition of self-referential information, leading to less efficient processing of incoming self-referential information. Results will be discussed in the context of the role of biased social cognition in the development of social competence, and how these concepts unfold over time.

**110.135 135** Qualitative Aspects of an Unstructured Unfamiliar Peer Interaction in Higher Functioning Children with Autism and Their Typically Developing Peers. D. R. Dajani*[1], L. V. Usher[1], C. A. Burrows[1], C. B. Schwartz[2] and H. A. Henderson[1], (1)*University of Miami*, (2)*Yale Child Study Center*

Background:

Despite average or above average cognitive abilities, higher functioning individuals with autism (HFA) display social deficits that significantly impact their adaptive functioning. These deficits are particularly apparent when children and adolescents with HFA interact with unfamiliar peers and can impact their ability to establish lasting and meaningful relationships (Bellini, 2004). While quantitative analyses reveal important information about the relations between social skills and outcomes, a qualitative approach offers a distinctive perspective on the unfolding of social interactions.

Objectives:

The aims of this study were: 1) to use a unique qualitative approach to examine aspects of an unstructured conversation between children with HFA and unfamiliar, typically developing (TD) peers on the dyad level, and 2) to examine differences in qualitative aspects between individuals with HFA and their TD peers.

Methods:

Children with HFA ($N$ = 39, 34 males, $M_{age}$ = 13.85, $SD$ = 2.80) were paired with a gender-, age-, and IQ- matched TD peer ($N$ = 39, 34 males, $M_{age}$ = 13.56, $SD$ = 2.01). Each dyad was given five minutes to "get to know each other." Interactions were transcribed and coded by two researchers, who have established reliability (κ = .63 - .98). We developed a novel coding scheme to assess qualitative aspects of these conversations. First, transcripts were segmented into personal topics (i.e., "I'm in tenth grade.") or factual topics (i.e., "So five minutes, that's pretty short."). A "turn" was defined as each sentence said during the conversation that offered unique content. Each turn was classified into one of four content areas: self-attributes, school, family, or friends. Finally, each turn was also classified as either appropriate or inappropriate for a social interaction in which one is first getting to know someone.

Results:

Preliminary analyses on 22 participants (11 dyads) revealed that at the dyad level, there was a mean of 12.91 segments initiated ($SD$ = 3.48). The majority of segment topics were self attributes (62%), followed by school (11%), family (7%), friends (7%), task-based factual (7%), and general factual (6%).

Individuals with HFA initiated more segment topics than TD participants, $t(20) = 3.91$, $p$ = .001. In addition, participants with HFA initiated significantly more factual topics, $t(19) = 2.79$, $p$ = .012, and TD initiated significantly more personal topics, $t(19) = 2.79$, $p$ = .012. Participants with HFA had a significantly higher proportion of inappropriate turns than did TD participants, $t(12) = 3.073$, $p$ = .01.

Conclusions:

During an unstructured opening conversation, children and adolescents with HFA tend to initiate changes in topics more than their TD peers, but their segment topics and turns in the conversation are not always appropriate to first getting to know someone. Future studies should combine qualitative and quantitative methods to examine inappropriate comments as predictors of parent-reported social competence in participants with HFA. By combining both methods, we can determine how content of opening conversations relates to social skills deficits in HFA and ultimately how this impacts social relationships between individuals with HFA and their peers.

**110.136 136** Recognizing Posed and Evoked Facial Expressions from Adults with Autism Spectrum Disorder. D. J. Faso*[1], N. J. Sasson[1] and A. Pinkham[2], (1)*University of Texas at Dallas*, (2)*Southern Methodist University*

Background: Successful social interaction requires both effective perception and expression of emotion. Although a large literature has demonstrated that social interaction deficits in Autism Spectrum Disorder (ASD) may result from impairments in emotion perception, comparably little research has assessed whether expression of emotion in ASD is less effectively interpreted by social others. The few prior studies investigating this question have assessed cued or posed expressions, which may fail to capture how facial expressivity naturalistically occurs when experiencing an emotional event.

Objectives: This study aimed to determine if posed and evoked facial expressions of emotion produced by adults with ASD are perceived differently by naïve observers compared to those produced by typically developing (TD) controls. Observers were predicted to 1) be less accurate in recognizing expressions from ASD adults (Emotion Recognition Accuracy; ERA), 2) rate ASD expressions as less intense, demonstrating 'flat affect', and 3) less natural. Further, the factors informative for correct identifications of emotional expressions were predicted to differ between the ASD and TD groups.

Methods: Static facial photographs of high-functioning adults with ASD (N=6) and typically developing (TD) comparison adults (N=6) were captured expressing five emotions (happy, sad, anger, fear, neutral) across varying intensities within both a posed and evoked condition. In the posed condition, participants produced expressions cued by the researcher. In the evoked condition, participants were coached to relive

emotional past experiences while their naturally elicited facial expressions were captured. Participants provided ratings of their subjective experience of emotion during the procedure. These ratings were higher in the evoked condition than the posed condition, validating the methodological efficacy of producing actual 'felt' emotions, but importantly did not differ between the groups ($F(1,8) = .596$, $p = .462$, $\eta^2 = .069$). In the second stage of the experiment, naïve observers (N=38) identified the expressed emotion in each photo, and rated the intensity and naturalness of the expression.

Results: Contrary to hypotheses, ERA was significantly higher for the ASD group than the TD group ($F(1,37)=4.557$, $p=.039$, $\eta^2 = .110$). However, ASD expressions were rated as significantly more intense ($F(1,37)=77.33$, $p<.001$, $\eta^2 = .676$) and less natural ($F(1,37)=118.703$, $p<.001$, $\eta^2 = .762$) than TD expressions. Intensity of expressions was correlated with ERA for both groups ($r=.55$, $p<.001$), and thus the significantly higher intensity ratings for the ASD group may have contributed to their higher ERA. Further, naturalness ratings in the evoked condition were related to ERA for the TD group ($r=.32$, $p<.05$) but not the ASD group ($r=-.03$, *n.s.*), suggesting that perceived naturalness facilitated ERA selectively for the TD group.

Conclusions: Higher ERA and intensity ratings for the ASD group compared to the TD group are inconsistent with notions of "flat affect" in ASD. Whether these unexpected results are specific to the sample under study here (high-functioning adults) is unclear. However, the higher intensity and naturalness ratings for the ASD group suggest patterns of atypical facial expressivity that may relate to broader social impairments. These findings persisted in the evoked condition suggesting that facial expressivity abnormalities in ASD extend to real world contexts.

**110.137 137** Scene Content Influences Dynamic Visual Scanning of Toddlers with and without ASD during Viewing of Naturalistic Videos. G. A. Marrinan*[1], S. Shultz[2], A. Klin[3] and W. Jones[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*

Background: When faced with complex, dynamically-unfolding social scenes, typically-developing (TD) toddlers effectively synchronize their viewing, converging on common locations more often than expected by chance. When viewing the same scenes, the visual resources of toddlers with ASD also converge significantly, but the locations and timing of this convergence differ relative to TD children. Previous research examining what drives visual attention of children with and without ASD has focused primarily on summary information about overall fixation to discrete regions-of-interest, such as eyes, mouths, bodies or objects, divorced from their dynamic social context. However, the importance and meaning of these regions-of-interest varies with the complex, ever-changing social interactions of which they are a part. In order to unpack how complex scene content drives visual attention, our laboratory has recently catalogued the occurrences of functionally meaningful social actions and physical elements within naturalistic videos. That investigation revealed that particular onscreen events, including emotional facial expressions and high amplitude vocalizations, were associated with significantly greater convergence among TD toddlers. However, factors guiding visual attention in ASD remain unknown.

Objectives: This study examines whether mechanisms driving attention in TD viewers (e.g. facial expressions and vocalizations of varying affect) guide or fail to guide visual convergence in toddlers with ASD.

Methods: Eye-tracking data were collected as TD toddlers (N = 44) and toddlers with ASD (N = 22) viewed naturalistic videos of peer interactions. Children were matched on chronological age and non-verbal function. We used kernel density estimation to quantify the level of convergence of visual scanning at each moment in time for each group separately. In parallel, we coded the occurrence of facial expressions (positive, neutral, and negative), and vocalizations (high and low amplitude) at each frame of the videos. We then used a generalized linear model to investigate how well each coded onscreen behavior predicted the level of convergence of visual scanning in TD toddlers and toddlers with ASD.

Results: TD toddlers' viewing patterns converged significantly 58.13% of the time, while toddlers with ASD converged significantly 28.36% of the

time. Results of the GLM revealed that negative facial expressions ($t(42) = 2.04$, $p = 0.048$), high amplitude vocalizations ($t(42) = 10.37$, $p < 0.001$), and low amplitude vocalizations ($t(42) = 2.66$, $p = 0.011$) predicted convergence among TD viewers. By contrast, only negative facial expressions ($t(15) = 3.24$ , $p = 0.005$) and low amplitude vocalizations ($t(15) = 3.93$ , $p = 0.001$) predicted convergence among viewers with ASD.

Conclusions: These findings provide an important step towards identifying specific scene content that guides or fails to guide visual attention in viewers with ASD. Future analyses will examine visual convergence with respect to a wider range of coded onscreen events. In addition, we will examine the broader context within which these onscreen events occur and the level of engagement of each viewer in relation to these onscreen events to further investigate what drives visual engagement in toddlers with ASD.

**110.138 138** Self-Esteem, Autism Symptoms, and Anxiety in Children and Adolescents with Autism Spectrum Disorders (ASD). L. Gilhooly*[1], S. Mahdavi[1], J. S. Beck[2], J. C. Matter[1] and M. Solomon[3], (1)*UC Davis MIND Institute*, (2)*UC Davis*, (3)*MIND Institute*

Self-esteem, autism symptoms, and anxiety in children and adolescents with autism spectrum disorders (ASD)

Background: In typical development (TYP), high self-esteem has been associated with many positive outcomes related to adaptive functioning, while low self-esteem has been associated with many negative ones including higher levels of social anxiety. Self-esteem in children and adolescents with ASD has been relatively understudied. Self-concept may develop atypically in such youths due to their impairments in social information processing, and therefore self-concept may exhibit a different relationship with anxiety than that found in TYP.

Objectives: The study had two main objectives: 1) to examine the association between self-esteem and social deficits in children and adolescents with autism spectrum disorders; 2) to examine the relationship between self-esteem and anxiety in youths with ASD.

Methods: Participants were 27 individuals aged 8-18 years (M:F ratio = 12:6) diagnosed with ASD based on the Social Communication Questionnaire (SCQ). They completed the Piers-Harris 2 (Piers, Harris, & Herzberg, 2002), and Screen for Child Anxiety Related Disorders (SCARED; Birmaher et al., 1995).

Results: 1) Total standard scores on the Piers-Harris ranged from 27 to 63 with a mean overall score within the normal range (M=46.259, SD=8.488). Of the six domains of self-esteem (Behavioral Adjustment, Intellectual and School Status, Physical Appearance and Attributes, Freedom from Anxiety, Popularity, Happiness and Satisfaction), the sample scored lowest and below age normed scores on Popularity, a measure of their social self-concept, and scored significantly higher on Happiness and Satisfaction ($t=3.086$, $p=0.007$, $df=7$). Popularity was positively associated with age ($r=0.413$, $p<0.05$). Greater social communication deficits as assessed by the SCQ were associated with lower levels of overall self-esteem ($r=-0.432$, $p=0.024$). 2) Participants with generalized, but not other forms of anxiety, had significantly lower self-esteem than those whose did not ($t=3.402$, $p=0.004$, $df=15.522$).

Conclusions: Although the population scored in the normal range for overall self-esteem, they exhibited below average scores on the Popularity domain of self-concept, suggesting that youths with ASD are concerned with how peers evaluate them. However, their score on the Happiness and Satisfaction subscale, which was found to be in the normal range, suggests there is a dissociation between their own social self-perceptions as indexed by the Popularity score and their overall well-being. Furthermore, scores in the Popularity domain increased with age. Also of clinical interest were findings that the presence of increased ASD symptoms and generalized anxiety were associated with poorer self-esteem. Future research is needed that better teases apart these relationships as they may have important implications for designing interventions that help adolescents with ASD.

**110.139 139** Sex Differences and Gender Stereotypes: An Analysis of School-Age Children with High-Functioning Autism. M. Dean*[1] and C. Kasari[2], (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

Background: Gender differences exist in the social relationships of typically developing children (Goodwin, 2002; Maccoby, 1999; Talbot, 2010), yet it unclear if the social behaviors of children with ASD are similar to their same gender peers,

or if gender differences exist in the way that boys and girls with ASD socialize.

Objectives: The purpose of this study was to examine the extent to which the social behaviors of girls and boys with ASD at school can be characterized as masculine, feminine, or neutral. This study also sought to explore whether or not there are qualitative differences in the social behaviors of girls and boys with ASD.

Forty-eight school-age girls with ASD and boys with ASD were matched by age (μ = 7.93 (1.25)), grade, IQ (μ = 93.94 (13.34)), and city of residence (girls: n=24; boys: n=24). To meet criteria for this study, children with ASD had to be without intellectual disability (IQ ≥ 70; confirmed by the Stanford-Binet Fifth Edition), and educated in the general education classroom for a minimum of 80% of the school day. The diagnosis of ASD was confirmed using the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2002). Data collected from typically developing populations (n=119) were used to triangulate the gender themes and to establish social norms for masculine, feminine and neutral behaviors.

Methods: This sequential mixed methods analysis (QUAL quan QUAL, including typology development; Teddlie & Tashakkori, 2009) is a secondary analysis of participant observation field notes that were collected at schools during unstructured social periods (recess, lunch, and nutrition).

Results: The descriptive statistics revealed that children with ASD endorsed masculine and feminine behaviors, yet both boys and girls with ASD experienced social challenges that interfered with their ability to fully participate in activities. Within the ASD sample, however, the social challenges varied by gender. Compared to boys with ASD, girls with ASD made more social initiations and were in closer proximity to social groups, which made them vulnerable to more rejection. In contrast, boys with ASD tended to be alone, and were more likely than girls to reject social invitations.

Conclusions: Because girls with ASD appeared more socially integrated than they actually were, it was more difficult to recognize their social challenges. In contrast, boys with ASD tended to be alone during recess, making their difficulties easier to detect. Modifications to social skills interventions at school are needed to better address the environmental factors that influence the social behaviors of boys and girls with ASD.

**110.140 140** Social Cognition Treatment: A Preliminary Investigation of Social Thinking in an Inpatient Setting. M. Siegel*[1], O. Teer[2], B. Ellsworth[2], B. Milligan[3], A. Stedman[2], T. Hutchins[4] and K. A. Smith[1], (1)*Maine Medical Center Research Institute*, (2)*Spring Harbor Hospital*, (3)*Spring harbor Hospital*, (4)*University of Vermont*

Background: Social communication impairment is a core deficit in individuals with Autism Spectrum Disorder (ASD). Challenges in reading non-verbal cues, inferring the intentions of others and interpersonal flexibility are universally present in the population. Historically, clinicians have addressed social communication impairments with discrete social skill interventions, such as teaching phrases and mannerisms in scripted social situations. These methods have not led to improvements in the flexible application of social cognition or generalizability to unscripted situations (Bellini, 2007). One approach to this challenge, "Social Thinking" (Winner, 2008) has been widely adopted in schools and other settings within the United States. Despite its popularity, there has been minimal research on the efficacy of this approach in improving social communication. There is also a lack of a manualized curriculum for clinicians to increase fidelity and replicability.

Objectives: The primary objective was to develop and implement a manualized Social Cognition Treatment (SCT) curriculum for children with ASD and/or Intellectual Disability (ID). Our secondary objective was to measure changes in theory of mind capacities in patients exposed to the SCT curriculum and examine for potential differences in theory of mind scores between patient groups (ASD, ASD+ID, ID).

Methods: Nine children hospitalized in a specialized child psychiatry unit with ASD by DSM IV-TR criteria and/or Mild Intellectual Disability (ID, FSIQ 54-70) participated in the SCT curriculum. The SCT curriculum was created by a multi-disciplinary team of clinicians and was designed to enhance theory of mind capacity in individuals with autism and/or intellectual disability by increasing perspective taking ability, encouraging more flexible thinking and enhancing coping strategies. The SCT curriculum requires dedicated participant involvement in 16 forty-five

minute sessions delivered over a 4 week period. Teacher responses on the Theory of Mind Inventory (ToMI;Hutchins, Prelock, & Bonazinga, 2012) were collected after a one-week observation period (baseline), and again at 2 weeks (mid-point) and 4 weeks (end-point) of the SCT sessions. Repeated Measures Analysis of Variance (RMANOVA) was used to examine changes in ToMI scores over time.

Results: The sample consisted of 9 males, two with ASD, three with ID, and four with ASD+ID, ages 6-18 (mean = 11.0 years) who completed an average of 14 of 16 SCT sessions. RMANOVA results indicated overall patient improvement in mean TOMI scores from baseline ($M$=14.90, $SD$= 3.06) to mid-point ($M$=15.90, $SD$=2.64) to end-point ($M$=16.45, $SD$=2.72), however this was not statistically significant, $F$(1.16, 9.31)=3.85, $p$=0.076. Examination of TOMI differences by diagnostic group revealed improvement in mean TOMI scores for ASD and ASD+ID patients, whereas ID only patients showed a slight decrease in TOMI scores over time.

Conclusions: Preliminary investigation of a newly developed group Social Cognition Treatment suggests that it may be related to improvements in a measure of theory of mind for children with ASD. Though we cannot suggest causality in this uncontrolled, open-label preliminary study, our findings may indicate that the SCT has a different effect for the ASD versus ID populations. Controlled study of the SCT in an outpatient ASD population would provide initial testing for efficacy.

**110.141 141** The Psychophysiological and Psychological Effects of Ostracism in ASD. E. M. Trimmer*, S. McDonald, D. Mathersul and J. A. Rushby, *University of NSW*

Background: Although individuals with an Autism Spectrum Disorder commonly experience social exclusion and ostracism at some stage in their lives, little is known about the way in which this is experienced.

Objectives: This study aims to examine and explore the psychological and physiological effects of ostracism in individuals with ASD compared with matched controls.

Methods: Nine individuals aged 16 or older (9 males; mean age 33.67 years) with a diagnosis of ASD and 11 matched controls (6 males, 5 females; mean age 26) participated in an online game of ball tossing, Cyberball. Each participant played two games, both against fictional players: one game in which they were excluded from the game and another in which they were included and the ball was shared equally between players. Whilst playing, participants' arousal level was monitored via skin conductance. Participants were also required to complete a self-report questionnaire about their experience and mood after both games.

Results: Individuals with ASD showed increased arousal compared with controls when playing the game ($p$ = .05), both when excluded and included. Both groups showed higher skin conductance response to being ostracized than when included ($p$ = .001). Furthermore, individuals with ASD did not demonstrate a reduction in arousal over the course of the game, as controls did. Psychological responses indicated that individuals with ASD showed similar patterns of responses to controls and shared the same social needs and mood.

Conclusions: The present findings suggest that individuals with ASD were more aroused and engaged in the game than controls, regardless of whether they were included or excluded. Individuals with ASD stayed focused throughout the game and did not disengage towards the end. No differences were found between the individuals with ASD and the control group in their perceptions of being ostracized. Individuals with ASD appeared to interpret negative feelings of exclusion and ostracism in a similar way to the control group.

**110.142 142** The Relationship Between Executive Dysfunction and Theory of Mind. C. Cantio*[1], S. J. White[2], J. R. M. Jepsen[3] and N. Bilenberg[1], (1)*University of Southern Denmark*, (2)*University College London*, (3)*Center for Neuropsychiatric Schizophrenia Research*

Background:

The cognitive dysfunctions and the possible relationship between especially Theory of Mind (ToM) and Executive Functions (EF) have recently received an increasing interest.

Russell (1) has suggested that EF is crucial in the development of ToM and that difficulties within EF may lead to failure in developing an understanding of mental states. This was

supported by Pellicano (2) who found that a competent EF could be seen without ToM-deficits, however, she was not able to find this the other way around.

White (3), on the other hand, has recently suggested that the reason individuals with ASD have trouble in EF-tasks may be caused by their disability to form an explicit understanding of the experimenter's expectations of the task (ToM).

Objectives:

The objective of this study was to examine the distribution of deficits in the different domains within the ASD group, and try to identity subgroups of ASD based on their cognitive style.

Methods:

Thirty-one clinically diagnosed high-functioning children with ASD were tested with two ToM tests; "Strange Stories" and "Animated Triangles", and with two different approaches to EF; "Generativity" with verbal instruction and answers (active experimenter, AE) and a CANTAB-battery covering a range of the classic executive tasks in a computerized version with very few verbal instructions (inactive experimenter, IE).

Results:

We found that about 65% of the ASD group had ToM-dysfunctions ($5^{th}$ percentile of a neurotypically developed, NTD, control group). Within EF we found that about 19% had problems in the AE tasks and only about 10% in the IE tasks (not significant compared to the NTD group).

There was a greater overlap to ToM-difficulties in the AE performance (with half of the group showing additional ToM difficulties), although numbers unfortunately were too small to analyse.

About 11% of the children displaying ToM difficulties had additional difficulties in the AE tasks in EF.

Conclusions:

These results indicate that children with ASD have more difficulties in primary verbal and person-oriented EF tasks compared to computerized, less verbal tasks. Data also indicate that only few ASD children with ToM problems have underlying executive dysfunctions. This slightly supports White's hypothesis about underlying ToM-disabilities, although we would have expected an even greater overlap.

To investigate the relation between ToM and EF further we need to separate the two cognitive functions in the tasks we use. Therefore we are now compiling a new battery of implicit/intuitive ToM tasks, where we have tried to minimize the executive demands. We will be able to present the first preliminary data from these ToM tasks at IMFAR 2014.


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**110.143 143** The Relationship of Social Cognition, Language, and Executive Function to Theory of Mind in Children and Adults with ASD. D. L. Williams*[1], M. E. Wendelken[1], H. Z. Gastgeb[2] and N. J. Minshew[2], (1)*Duquesne University*, (2)*University of Pittsburgh School of Medicine*

Background: Whereas it is generally accepted that individuals with autism spectrum disorders (ASD) have deficits in theory of mind (ToM), or the ability to understand that other people have thoughts and to infer or predict what those thoughts might be, the relationship of this deficit to other aspects of ASD, particularly social cognition, language, and executive function is still debated. Previous studies have been limited by only examining one or two of these cognitive abilities in relationship to ToM, in a limited number of participants, and/or in only including children or adults in the sample.

Objectives: The current study examined the relationship of measures of social cognition and language/verbal ability to measures of ToM in a

large sample of 272 children and adults with ASD ranging in age from 6 to 53 years. In addition, large subgroups of children and adults within this sample had received the same executive function measures of working memory and cognitive flexibility making it possible to examine relationships between these variables to ToM in cohesive set of individuals.

Methods: The primary dataset contained 272 participants with ASD (166 individuals ages 5 to 15 years and 106 individuals ages 16 to 53 years) mean age 16.2 (SD = 7.9; range 6.0 to 53.8). It included 239 males and 33 females with mean VIQ 104.7 (SD = 14.5; range 73 to 141), mean PIQ 106.3 (SD = 14.5; range 66 to 144), and mean FSIQ 106 (SD = 13.9; range 73 to 146). Three hypotheses of the relationship between the variables were examined using two different versions of three different hierarchical multiple regression models. The ToM measure was the outcome or predicted variable. Two different ToM measures were used as dependent variables: 1) an aggregated measure from the traditional *Sally and Anne, John and Mary*, and *Peter and Jane* tasks; and, 2) the *Reading the Mind in the Eyes Test-Revised.* Independent variables included measures of social cognition (from the ADOS & ADI-R), language ability, verbal and spatial working memory, and cognitive flexibility, which were entered at different steps of the analyses based on the predictive model that was being tested. Age was entered as a control variable in all of the models.

Results: A series of hierarchical linear regression models indicated that the strongest relationship occurred between language ability (as measured by Verbal IQ) and performance on both the traditional ToM measures and the Eyes test. Social cognition abilities were a greater predictor for ToM in children than adults with ASD, but these abilities were not the primary predictor. No executive functioning measures were revealed to be significant predictors of ToM ability in ASD for either the children or adults.

Conclusions: In both children and adults with ASD, ToM abilities appeared to be related to overall language abilities rather than a more generalized ability in social cognition or executive function. This relationship occurred both for ToM as derived from traditional measures which are more language dependent and for ToM as derived from the Eyes test, a task which is less language-dependent.

**110.144 144** The Relationships Between Perception-Action Skills and Social Skills in Young Children with Autism. A. Hellendoorn*[1], L. Wijnroks[1], E. Van Daalen[2] and P. Leseman[1], (1)*Utrecht University*, (2)*University Medical Centre*

Background: Children with autism spectrum disorder (ASD) are characterized by impairments in social interaction and communication (APA, 2000). In addition, these children are known to perceive and act upon their environment differently (e.g. Gepner & Féron, 2009). According to an embodied embedded cognition account being socially skilled requires being adept at picking up the relevant information and being able to produce adequate real-time actions (Good, 2007; Smith & Gasser, 2005; Thelen, 2000). Several authors have suggested using a more embedded embodied approach to social cognition in general (Gallagher, 2008) and to study the social skills in autism specifically (DeJeagher, 2013). This implies taking into account the role of perception-action processes for when studying the development of social skills.

Objectives: The purpose of this research is to determine whether perception-action skills and social skills are related in young children with autism.

Methods: Forty children, 32 boys and 8 girls, with a mean age of 34 months (SD 9 months), were included in this study. Perception-action skills was assessed by (1) the sum of the scores on the visual reception and fine motor subscales of the Mullen Scales of Early Learning and (2) the number of months the child could walk unaided at the time of the ADOS-assessment. Social skills were measured by coding the initiation of social interaction on videotaped observation of the ADOS. Regression analyses were conducted to determine the relationship between perception-action skills and social skills.

Results: A significant positive relationship was found between (both measures of) perception-action skills and social skills, with a medium effect size.

Conclusions: The present study indicates a positive relationship between perception-action skills and social skills. This suggests that perception-action skills play a role in the

acquisition of social skills in young children with autism. More longitudinal research with both typically and atypically developing groups is needed to confirm and specify this relationship. This may eventually enhance understanding the developmental trajectories of ASD and lead to a more central role of perception-action processes and a consideration of cascades across developmental domains in screening, diagnostic and intervention procedures.

**110.145 145** Visual Interest for Biological Motion and Correlation to Early Social Behaviours in Young Children with ASD. M. Franchini*, H. Wood de Wilde, B. Glaser, E. Gentaz, S. Eliez and M. Schaer, *University of Geneva*

Background:

According to the social motivation theory of autism (Chevallier et al., 2012), the lack of social interest and orientation to social stimuli explains part of the symptomatology of individuals with autism spectrum disorder (ASD). These symptoms are expressed in several ways as the avoidance of eye contact or a reduction of joint attention behaviours (JAB). Measuring the lack of orienting on social relevant stimuli with eye-tracking (ET) could be an interesting way to discriminate between ASD and typically developing (TD) young children's visual pattern and to predict behavioural deficits in ASD individuals.

Objectives:

The aim of the study is to define a social phenotype for ASD by using visual interest on social stimuli (biological motion) vs. geometric objects (non-biological motion). Moreover, we aim at exploring the correlation between the lack of interest on social stimuli in ASD individuals and their symptoms's severity.

Methods:

On the basis of Pierce and colleagues ET paradigm (2011), a split screen with biological motion and non-biological motion was presented. Images were both presented at the same time. Using the Autism Diagnostic Observation Schedule (ADOS, Lord & Spence, 2006) and the Early Social Communication Scale (ESCS, Mundy et al., 2003), we also investigated the correlation between visual preference for non-biological motion and symptoms severity. Twenty children with ASD (mean age= 3.36±1.78), and 15 typically developing children (mean age= 3.77±1.69) were evaluated.

Results:

The Student's t-test showed a significantly higher interest for non-biological motion in children with ASD compared to NT ($t=3.174$, $p<0.01$). Moreover, this interest correlates with ADOS Communication Score ($r=0.706$, $p<0.01$) but not with ADOS Repetitive Behaviours Score ($r=0.382$, $p>0.05$). Further correlation demonstrated that the preference for non-biological motion could predict the lack of JAB in the ESCS ($r=0.658$, $p<0.05$).

Conclusions:

Our results further confirm a good discrimination between ASD and TD children in visual preference for social stimuli vs. geometric objects. The significant correlation between interest for geometric motion and the severity of symptoms on communicational deficits and JAB further strengthen the social motivation hypothesis in autism.

**110.146 146** Why Is Impaired Social-Acting Understanding Associated with Autism? Evidence for a Unique Role of Ingroup-Support Motivation. R. Baillargeon*[1] and D. Yang[2], (1)*University of Illinois*, (2)*Yale University*

**Background:** Individuals with more autistic traits are less able to understand social acting, the well-intentioned social pretense adults routinely produce to maintain positive relationships with their ingroup (e.g., friends, coworkers, relatives). Social acting can take the form of white lies, false cheer, prevarication, tactful omissions, and so on. Questions have been raised about the mechanisms underlying the impairment in social-acting understanding in autism. One possibility is suggested by recent research on the moral principle of ingroup-love and its corollaries, ingroup-support and ingroup-loyalty. If social acting is intended to support one's ingroup by maintaining positive interactions, then individuals with poorer ingroup-support motivation (ISM) might be less likely to view social acting as appropriate. If individuals with more autistic traits have weaker ISM, it might explain their difficulties with social-acting understanding.

**Objectives:** We aimed at testing the hypothesis that ISM mediates the link between autistic traits

and social-acting understanding, while comparing and contrasting the role of ISM with seven other theoretically plausible mediators: social desirability, need to belong, and five distinct moral foundations (care/harm, fairness/cheating, loyalty/betrayal, authority/subversion, and sanctity/degradation).

**Methods:** Study 1 included 133 adults recruited through Amazon Mechanical Turk (60 women and 73 men, mean age = 31.96), who received the following measures: (a) social-acting understanding (Yang & Baillargeon, 2013); (b) Autism Spectrum Quotient (Baron-Cohen et al., 2001); (c) social desirability (Crowne & Marlowe, 1960); (d) need to belong (Leary et al., 2013); (e) moral foundation questionnaire (Graham et al., 2011); and (f) a new ISM measure developed for this study, which assesses how important it is to support (e.g., to help, comfort, or cooperate with) one's ingroup. Study 2 included 266 adults again recruited through MTurk (150 women and 116 men, mean age = 34.94), who received (a) the social-acting understanding measure from Study 1; (b) Broad Autism Phenotype Questionnaire (Hurley et al., 2007); and (c) one of two versions of ISM (with ratings from the first- or third-person perspective).

**Results:** Study 1 showed that autistic traits were correlated with weaker social-acting understanding (replicating previous results) as well as with lower ISM, weaker social desirability, and lower reliance on care/harm morality. Among these last three factors, only ISM and the compassion/empathy aspects of care/harm morality significantly mediated between autistic traits and social-acting understanding; when gender was controlled for, only ISM was a significant mediator. Using a larger sample and different measures of autistic traits and ISM, Study 2 replicated and generalized the mediating effect of ISM.

**Conclusions:** The current results indicate that weak ingroup-support motivation is a key mechanistic explanation for the autistic impairment in social-acting understanding. Individuals with more autistic traits show a weaker motivation to actively support ingroup members, including the motivation to maintain positive interactions, which in turn explains their difficulties in appreciating social acting. The findings substantially extend the literature on social-motivation deficits in autism and raise an important issue in ASD that has received little attention to date.

**110.150 150** Predictors of Growth in Communication Complexity over 16 Months for Children with ASD. H. Huber*, S. Goldman and P. J. Yoder, *Vanderbilt University*

Background: One of the core deficits of autism spectrum disorder (ASD) is in the area of communication. As a result children with ASD often struggle to develop early language skills, interact with others, and form relationships with both peers and adults. The importance of understanding the trajectory of communication development cannot be understated due to the role of communication in future social and academic progress. Research also shows that play (e.g., toy play, symbolic play), joint attention (i.e., sharing attention, following and directing the attention of others), and imitation are strong correlates with later language skills (Kasari, Freeman, and Paparella, 2006; Toth, Munson, Meltzoff, & Dawson, 2006). The frequency of intentional communication that is weighted by the complexity of the form (lower weight for nonverbal and highest weight for multi-word) used to communicate has been shown to grow in a positive linear or quadratic fashion during the nonverbal to early multiword stages of communication development in typically developing children and in infant siblings of children with ASD (Yoder, Stone, Walden, Malesa, 2009). Growth of weighted intentional communication has not been model, nor have its correlates been identified, in children with ASD.

Objectives: Do measures of play, imitation, and communication positively co-vary with growth curves of weighted intentional communication (WIC) of participants 16 months after study entry, controlling for IQ and ADOS social communication algorithm?

Methods: Our participants included 86 pre-school initially nonverbal or minimally-verbal children with a diagnosis of ASD. Their scores on the ADOS diagnostic algorithm ranged from 6 to 28 with a mean of 22.57 (SD=3.85). Standard scores on the Mullen Scales of Early Learning ranged from 49 to 122 with a mean of 51.56 (SD = 8.49). A measure of WIC was taken at 5 time-points, each 4 months apart. Weighting was accomplished by assigning one point to nonverbal communication, two points to single word

communication, and three points to multi-word communication. All predictors were measured at Time 1. Communication was measured using scales 4-7 of the Communication and Symbolic Behavior Scale (CSBS; Wetherby & Prizant, 1993). Imitation was measured using Motor Imitation Scale (MIS; Ousley & Littleford, 1997), and number of differentiated play activities was measured from the Development Play Assessment (DPA; Lifter, 2000). Mixed level modeling was used to test whether play, imitation, and communication accounted for unique variance in growth of WIC. ASD severity and cognitive impairment levels were analyzed as control variables.

Results: Preliminary analyses indicate that play action diversity, motor imitation, and communication predicted growth of WIC over the 16-month period, even after controlling for severity of autism and IQ.

Conclusions: Play skills, motor imitation, and measures of communication are important predictors of growth in WIC for young children with ASD. These results can be used to focus interventions on specific skill areas for these children.

## 111 Animal Models / Epidemiology

*Organizer:* A. Reichenberg *Mount Sinai School of Medicine*

**111.001** A Novel Shank3-Deficient Rat Model to Understand the Neural Basis of Autism. H. Harony-Nicolas*[1], O. B. Gunal[1], R. Gur[2], K. Casten[1], N. P. Daskalakis[1], A. N. O'Toole[3], S. A. Dick[1], S. Wagner[2], M. G. Baxter[1], M. Shapiro[1] and J. D. Buxbaum[4], (1)*Icahn School of Medicine at Mount Sinai*, (2)*University of Haifa*, (3)*Trinity College Dublin*, (4)*Seaver Autism Center for Research and Treatment*

**Background**: Shank3 is a scaffolding protein that forms a key structural part of the postsynaptic density (PSD) of excitatory synapses, where it recruits glutamate receptors and binds cytoskeletal elements regulating glutamate signaling. Haploinsufficiency of SHANK3 causes a monogenic form of autism spectrum disorders (ASD). Characterization of mouse models with *Shank3*mutations provided evidence for impaired glutamatergic synaptic function in hippocampal and striatal brain slices and deficits in several behavioral measures related to ASD. Yet, our knowledge about the affected molecular pathways and the alterations in brain circuitries and their relation to the behavioral deficits observed in ASD remains incomplete.

**Objectives**: The aim of our study is to analyze the effect of Shank3 deficiency on ASD associated behaviors and to uncover the alterations in synaptic plasticity in brain regions and circuits associated with the impaired behaviors. At the molecular level, we aim to identify the affected pathways that underlie the behavioral and synaptic deficits. To achieve our aims, we have developed a genetically modified rat model with a targeted disruption of *Shank3*and completed a battery of behavioral, biochemical, electrophysiological and genome wide expression analyses.

**Methods**: *Behavior:* To study social behavior, we applied a battery of social behaviors tests including long and short-term social recognition memory (SRM). To evaluate attentional function and behavioral flexibility, we used the 5-choise serial reaction time (5-CSRT) task and a strategy-shifting paradigm, respectively. *Electrophysiological recording*: To analyze synaptic function and plasticity we used in vitro recording from acute hippocampal brain slices. To study the long-range synaptic connectivity in the Hippocampal-medial prefrontal cortex (mPFC) circuitry, we stimulated the hippocampus and recorded the synaptic responses in the mPFC in anesthetized rats. *Genome wide expression and pathway analysis*: We used proteomic approaches and RNA sequencing technology to compare gene expression signatures between the *Shank3*-deficient rats and their WT littermate and applied gene ontology (GO) analysis to reveal the affected molecular pathways.

**Results:** Behaviorally, we found that *Shank*-deficient rats are impaired in long-term SRM, attention, and reversal learning (an essential component of behavioral flexibility), all of which are prevalent in subjects with ASD. These behaviors are highly dependent on the intact function of brain regions previously associated with ASD, i.e., the hippocampus and the PFC. Our *in vitro* recordings demonstrated impairment in long-term potentiation (LTP) and depression (LTD) in the hippocampus while *in vivo* recordings showed impaired mPFC LTP in response to hippocampal stimulation. Proteomics analysis

revealed decreased levels of postsynaptic components, including Homer and PSD-95, while genome wide expression and GO analysis revealed a list of differentially expressed genes in *Shank3*-deficient rats highly enriched in pathways and cellular components involved in cell communication, extracellular matrix (ECM) receptor interaction and focal adhesion.

**Conclusions**: Shank3 deficiency has an effect on behaviors relevant to ASD and modulates synaptic plasticity in brain regions and circuits underlying them. These deficits could be in part due to the disruptive effect of Shank3 deficiency on ECM-associated factors that are known to play a critical role in synaptic plasticity and in forming neuronal connections during development.

**111.002** Shank2 Mutation in a Rat Model Induces Behavioral, Molecular and Electrophysiological Alterations Consistent with an ASD-like Phenotype. M. E. Modi*[1], D. Reim[2], M. J. Schmeisser[2], T. M. Boeckers[2], S. J. Sukoff Rizzo[1] and D. L. Buhl[1], (1)*Pfizer Inc.*, (2)*Institute for Anatomy and Cell Biology, Ulm University*

Background: A number of the genes identified as anomalous in genetic screens of the autism spectrum disorders (ASD) population code for proteins that regulate synaptic plasticity, including the *Shank* family of genes. The link between mutation of these ubiquitously expressed genes and the selective social impairments and repetitive behaviors featured in ASD, though, is still unclear. Transgenic introduction of mutations identified in human ASD subjects into rodent models enables the association of specific genotypes to phenotypes. Rat models present several advantages over mouse models for characterizing ASD mutations due to their rich social behavioral repertoire, metabolic similarities to humans and amenability to complex electrophysiological manipulations.

Objectives: To investigate the relationship between decreased synaptic function and social impairment, we have characterized the behavioral, molecular and electrophysiological phenotype of rats expressing a mutation of the *Shank2* gene associated with ASD. The characterization of neural activity associated with aberrant behavior has the potential to identify reliable biomarkers of both disease and drug response.

Methods: Transgenic Sprague-Dawley rats containing a targeted deletion of exon 31 of the SHANK2 gene were generated using zinc finger nuclease technology. The subsequent animals were characterized through a behavioral battery, molecularly, through western blot protein quantification of regional synaptosomal brain homogenates, and electrophysiologically, through in vivo, chronically implanted, surface and depth electrodes.

Results: Mutation of the *Shank2* gene results in alterations in social behavior seen throughout development. Homozygous *Shank2* mutant rats (HOs) engage in less species typical juvenile play than wild type rats (WTs). This deficit is maintained into adulthood as evidenced by decreased social investigation of conspecifics and transmission of food preference. However, *Shank2* mutation in the rat, unlike in the mouse, does not result in decreased social approach. HOs also exhibited several forms of restricted and repetitive behaviors analogous to those observed in ASD, including increased locomotion and abnormal circling and checking behaviors. Uniquely, HOs also show increased motivation in a progressive ratio task that is independent of hyperactivity. The behavioral deficits associated with *Shank2* mutation are accompanied by upregulation of Shank3 and mGluR1 in the striatum and downregulation SHANK1 and Homer1 in the hippocampus. Local field potential recordings in multiple nodes of the social brain circuit, including the amygdala, entorhinal cortex and hippocampus were collected to assess differences in network activity resulting from *Shank2* mutation.

Conclusions: *Shank2* mutation in the rat model recapitulates many of the behavioral features of ASD and has broad effects on the expression of synaptic proteins. Exploration of electrophysiological phenotypes associated with these behaviors in this model may shed light on the neural underpinnings of the symptomatology of the disorder.

**111.003** Identification of Critical Periods for Treatment of Autistic Behavior in Purkinje Cell Tsc1 Mice. P. Tsai*, *Boston Children's Hospital*

Background:

Cerebellar Dysfunction has been implicated in the pathogenesis of autism spectrum disorders. By generating a mouse model where *Tsc1*is deleted

specifically in cerebellar Purkinje Cells, we have recently demonstrated that cerebellar dysfunction is sufficient to generate abnormal autistic behaviors and that early treatment with the mTOR inhibitor rapamycin can prevent the development of cerebellar pathology and autistic-like behavior.

Objectives:

Evaluate the benefits of later rapamycin treatment on autistic-like behaviors and to delineate critical periods of treatment for autistic-like behaviors.

Methods:

Using our Purkinje Cell *Tsc1*mouse mutants, we have investigated the impact of rapamycin treatment initiated during adulthood on behavior, pathology, and electrophysiologic function to delineate the critical periods of treatment of autistic behavior.

Results:

With rapamycin treatment starting at 6 weeks, we have demonstrated rescue of motor learning deficits and social behaviors – but not repetitive behaviors or cognitive inflexibility – in Purkinje Cell *Tsc1*mutant mice. Rapamycin treatment at this time point also rescues pathologic and electrophysiologic deficits in these mice. Later initiation of treatment at 10 weeks results in continued rescue of motor learning, but with inability to rescue social or repetitive behaviors. Moreover, pathologic deficits are also not ameliorated with treatment at this time point.

Conclusions:

These findings demonstrate that later treatment – even into adulthood – might offer benefit for social impairments. Furthermore, we demonstrate a critical period for treatment of social behaviors that differs from the critical period of rescue for motor learning, repetitive behaviors, and cognitive inflexibility, providing a platform for investigating the mechanisms underlying the critical periods for these behaviors and for further investigating the cerebellar contribution to autistic behavior.

**111.004** Language-Relevant Auditory Processing in the Cntnap2 Knockout Mouse. B. C. Castelluccio*, A. R. Rendall, D. T. Truong, I. M. Eigsti and R. H. Fitch, *University of Connecticut*

Background: The investigation of genetic variants that contribute to autism spectrum disorder (ASD) is critical for understanding the neurodevelopmental basis of the disorder. The gene contactin associated protein-like 2 (*CNTNAP2*) has been linked to both ASD and specific language impairment. *CNTNAP2* is located on chromosome 7q35 and encodes a cell adhesion protein that regulates signal transmission at the synapse. It is directly regulated by *FOXP2*, a transcription factor associated with language development. Additionally, *CNTNAP2* is highly expressed in language relevant cortical areas. To better understand the behavioral and biological mechanisms of ASD, a transgenic mouse model was recently generated with a genetic knockout of *Cntnap2*, the rodent homolog of *CNTNAP2*. Studies of this knockout model describe ASD-like symptoms, including poor social interactions, behavioral perseveration, and reduced vocalizations (Peñagarikano et al. 2011). However, language-relevant, low-level auditory processing in the knockout model has not previously been characterized. Recent evidence suggests that humans with ASD have impaired temporal auditory processing (Bhatara et al. 2013) and enhanced pitch discrimination (Eigsti & Fein 2013; Mottron et al. 2006; Bonnel et al. 2003), both features that may disrupt typical language development. That is, individuals with ASD show difficulty with some temporal aspects of auditory processing, but enhanced discrimination of spectral cues.

Objectives: The aim of the current study was to assess language-relevant intermediate phenotypes in the *Cntnap2*knockout model, targeting rapid temporal auditory processing and pitch discrimination abilities.

Methods: Twenty-two male *Cntnap2* knockout (KO) and 23 male wild type C57BL/6 (WT) mice were assessed. The groups were identical in age. A modified pre-pulse inhibition paradigm was used to examine attenuation of the acoustic startle response to a startle eliciting stimulus (SES) in the context of various auditory cues. Two acoustic tasks were performed. A "silent gap" task measured temporal aspects of auditory processing by examining the subjects' ability to detect variable duration silent gaps within continuous white noise. In this task, the cue for the SES was a silent gap. An "embedded tone" task measured spectral characteristics of auditory processing by

examining the subjects' ability to detect brief changes in frequency embedded within a continuous background pure tone. In this task, the cue for the SES was a frequency change.

Results: KO mice exhibited significant *deficit*s relative to WT in rapid auditory processing in the temporal silent gap task ($F(1,40)=6.29$, $p=.016$). However, KO mice exhibited significantly *enhanced* pitch discrimination in the spectral embedded tone task ($F(1,40)=9.39$, $p=.004$).

Conclusions: The pattern of impairment and enhancement seen in the *Cntnap2* KO mouse matches the pattern seen in humans with ASD. These findings suggest that *CNTNAP2* may play a role in development of low-level auditory processing features that contribute to human language and that aberrant *CNTNAP2* may be responsible for language atypicalities in individuals with ASD.

**111.005** A New Vasopressin V1a Antagonist Reveals a Brain Network Involved in the Symptomatology of the Rat Valproate Model of Autism. C. Grundschober*, T. Mueggler, C. Risterucci, F. Knoflach, P. Schnider and B. Biemans, *F. Hoffmann-La Roche, pRED, Pharma Research & Early Development*

Background: The use of the anticonvulsant drug valproate during pregnancy increases the risk for development of autism in children, accordingly the rat valproate model of autism has neuroanatomical and phenotypical similarities to human autism. A single injection of valproate to pregnant dams at days 12.5 of gestation, the time of the neural tube closure, induces a range of behavioral abnormalities in the offspring, such as deficits in social behavior, working and spatial memory and increased locomotor activity.

Objectives: With oxytocin, vasopressin is a neuropeptide thought to play an important role in regulating social behavior. We therefore wanted to investigate the role played by vasopressin in the phenotype of the rat valproate (VPA) model of autism.

Methods: Rats prenatally exposed to VPA were treated from postnatal day 60 daily for 3 weeks with a new, brain penetrant, vasopressin V1a receptor-specific small molecule antagonist. Their behavior was assessed in the Morris water-maze and in the 3 chamber social interaction test. Another group of VPA rats and wild-type controls was scanned by functional magnetic resonance imaging at postnatal day 60 and after 3 weeks chronic V1a antagonist treatment, to reveal changes in brain perfusion due to prenatal exposure to VPA and potential normalization by V1a antagonism.

Results: Chronic treatment for 3 weeks with our vasopressin V1a receptor-specific small molecule antagonist, completely reversed the impairments in social behavior, spatial memory and learning typically seen in VPA rats. In functional magnetic resonance imaging VPA rats are characterized by reduced brain perfusion in cortex, inferior colliculus, raphe, hippocampus and hypothalamus and increased brain perfusion in VTA, dorsal striatum and posterior hippocampus compared to control rats. Chronic V1a antagonism specifically normalized brain perfusion in dorsal striatum, VTA and colliculus.

Conclusions: These data show that chronic inhibition of vasopressin V1a receptors rescues normal behavior in VPA rats by normalizing perfusion in a brain network important for salience detection, sensory processing and reward. These results suggest that V1a antagonists have the potential to improve social interaction deficit in autism, a core symptom for which there is currently no drug treatment.

**111.006** Cord Blood DNA Methylation and Autism Observational Scale for Infants (AOSI) Score at 12 Months in the Early Autism Risk Longitudinal Investigation (EARLI). K. M. Bakulski*[1], J. I. Feinberg[1], S. C. Brown[2], C. Ladd-Acosta[1], C. J. Newschaffer[3], L. A. Croen[4], I. Hertz-Picciotto[5], R. Landa[6], S. E. Levy[7], A. P. Feinberg[1] and M. D. Fallin[2], (1)*Johns Hopkins University*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Drexel University School of Public Health*, (4)*Kaiser Permanente Northern California*, (5)*UC Davis MIND Institute*, (6)*Kennedy Krieger Institute*, (7)*Children's Hospital of Philadelphia*

Background: Both genetics and environmental exposures confer risk of autism spectrum disorders (ASD), though limited precise factors responsible for increased risk have been identified. Epigenetic state is controlled by a combination of environmental and genetic inputs and preliminary work implicates epigenetics in ASD, but no genome-wide assessment of DNA methylation prior to disease onset has been completed.

Objectives: To determine the relationship between DNA methylation at birth and scores on

the Autism Observational Scale for Infants (AOSI) at 12 months.

Methods: In the Early Autism Risk Longitudinal Investigation (EARLI), an ASD-enriched birth cohort, genome-scale infant cord blood DNA methylation was assessed on the Illumina 450k HumanMethylation array and compared to AOSI score at 12 months.

Results: AOSI total scores ranged from 0-20 (mean=5.4) for 94 infants with paired AOSI and methylation data available. Methylation data from blood cell sorted reference samples were used to estimate cord blood cell type proportions. General linear models adjusting for sex, cell type proportion, and surrogate variables for laboratory batch were applied to identify AOSI-specific differentially methylated positions as well as bump-hunting analyses, with the same covariates, to identify for differentially methylated regions.

Conclusions: The association between infant cord blood DNA methylation with AOSI score at several genomic regions will be described. Replication in additional populations is needed to test the utility of DNA methylation marks in predicting ASD or understanding ASD mechanisms.

**111.007** Increased Risk of Autism Spectrum Disorders at Short and Long Interpregnancy Intervals in a Finnish Population-Based Study. K. Cheslack-Postava*[1], A. Suominen[2], E. Jokiranta[2], V. Lehti[2], I. W. McKeague[1], A. Sourander[2] and A. S. Brown[3], (1)*Columbia University*, (2)*University of Turku*, (3)*Columbia College of Physicians and Surgeons*

Background: The time interval between completion of one pregnancy and conception of the next has the potential to influence prenatal exposures. Both short and long interpregnancy intervals (IPI) are believed to present possible adverse conditions for fetal development of the subsequent pregnancy. Short IPI has recently been associated with increased risk of autism, but whether long IPI increases risk for autism spectrum disorders (ASD) has not been thoroughly investigated.

Objectives: To test the hypotheses that both short and long IPI are associated with increased risk of ASD.

Methods: This study was conducted in the Finnish Prenatal Study of Autism, which is based in a national birth cohort. Children born in Finland in 1987-2005 and diagnosed with childhood autism, Asperger syndrome, or pervasive developmental disorder, not otherwise specified (PDD-NOS) by 2007 were identified through the Finnish Hospital Discharge Register. Matched controls were selected for each case using the Finnish Medical Birth Register. Non-firstborn subjects (2208 ASD cases and 5163 matched controls) were included in the primary analysis. IPI was calculated as the difference between the birthdates of each subject and their preceding sibling, minus gestational age of the subject. The association between IPI and ASD was determined using conditional logistic regression and adjusted for potential confounders. Analyses were also conducted stratified by ASD subtype and by presence of intellectual disability (ID) in the case.

Results: Relative to births with an IPI of 24-59 months, those with the shortest IPI (<12 months) had an increased risk of ASD (OR (95% CI), 1.50 (1.28, 1.74)) in confounder-adjusted models, while the ORs (95% CI) for longer IPI births (60-119 months and >120 months) were 1.28 (1.08, 1.52) and 1.44 (1.12, 1.85), respectively. Upon stratifying by ASD subtypes, the association of shorter IPI with ASD appeared to be accounted for by childhood autism and PDD-NOS, but not Asperger syndrome. However, the association of longer IPI with ASD was strongest and statistically significant only for Asperger syndrome. The association between IPI and ASD did not differ significantly between cases with versus without ID.

Conclusions: This study provides evidence that risk of ASD is increased at long as well as short IPI.

**111.008** Neonatal Blood Levels of Growth Factors and Pleiotropic Cytokines in Association with Autistic Disorder: A Danish Population-Based Case-Control Study. E. T. Parner[1], N. Larsen[2], M. Overgaard[1], D. Hougaard[2], J. Olsen[1] and D. E. Schendel*[1], (1)*Aarhus University*, (2)*Statens Serum Institut*

Background: Both agnostic and targeted biomarker investigations have been conducted for associations with autism, commonly targeting the inflammatory pathway hypothesized to contribute to autism pathogenesis. Cytokines, components of immune system function and investigated as markers of prenatal infectious or inflammatory risk for autism, can function also as growth factors during development and in the mature organism. Growth factors act as signaling molecules between

cells, stimulating cell growth, proliferation, differentiation and maturation and are important for regulating cellular processes. There are many large families of growth factors, such as the neurotrophins which include brain-derived neurotrophic factor (BDNF) investigated in relation to autism.

Objectives: Conduct a population-based case-control study of autistic disorder (AD) in association with neonatal levels of growth factors and pleiotropic cytokines measured in peripheral blood samples as indicators of abnormal or disrupted developmental and homeostatic processes, including immune activation, in the perinatal period.

Methods: The study cohort was comprised of all singleton Danish births from 1 January 1997 through 31 December 2003 identified in the Danish Medical Birth Register. Diagnoses of AD and perinatal and parent characteristics were obtained from the Psychiatric Central Research Register and Medical Birth Register. Study resources restricted the final sample to 550 randomly selected AD cases, matched in proportion on birth year to an existing control sample of 880 randomly selected cohort births. The biomarker panel was derived from a literature review for growth factors and pleiotropic cytokines reported to potentially affect neurodevelopment, especially autism. Based on multiplexing feasibility, a final panel of 19 biomarkers was developed. Measurements were performed on neonatal dried blood spots archived in the Danish Neonatal Screening Biobank. Case-control median biomarker levels, overall and by various strata, were compared using Tobit regression on the logarithm of the biomarker level and logistic regression was used to assess case-control differences in dichotomous variables defined on the basis of the 20th or 80th centile cut-offs of the control group distribution for each biomarker. Recursive partitioning was used in a combined analysis of all biomarkers to detect biomarker combinations which best discriminated cases and controls.

Results: Compared to control children, children with AD were more likely to have neonatal brain-derived neurotrophic factor levels below the 20$^{th}$ centile (adjusted odds ratio 1.56, 95% confidence interval 1.13-2.16) and IL-3 levels above the 80$^{th}$ centile (adjusted odds ratio 1.58, 95% confidence interval 1.12-2.23) and less likely to have leptin levels above the 80$^{th}$ centile (adjusted odds ratio 0.50, 95% confidence interval 0.35-0.70). From recursive partitioning, the combination of leptin levels below the 24$^{th}$ control centile and ciliary neurotrophic factor levels above the 8$^{th}$ control centile level discriminated cases from controls with 32% more cases than expected.

Conclusions: Small, but possibly discriminatory, shifts in neonatal peripheral blood levels of pleiotropic neurotrophic, neuroendocrine and immunomodulatory factors were observed to be associated with AD. Although these findings may reflect altered immune modulation in newborns later diagnosed with AD, alterations in multiple developmental networks may be implicated.

**111.009** Placental Structure in ASD: Does the Placenta Mirror the Diagnosis?. C. M. Salafia*[1], C. Platt[2], T. Girardi[1], R. Shah[3], G. Merz[1] and D. P. Misra[4], (1)*Institute for Basic Research*, (2)*University of Bristol Hospitals*, (3)*Placental Analytics*, (4)*Wayne State University*

Background: The placenta is a fetal organ regulated in utero by fetal genes, but which is responsive to and may be altered by stressors in the maternal environment in which it grows and matures.

Objectives: We have speculated that the shape of the placenta, a vascular fractal, may be measurably altered in ASD cases as compared to controls.

Methods: Placentas from the Avon Longitudinal Study of Parents and Children were processed according to a standard protocol and photographs obtained of the fetal chorionic plate and serial slices of the placental disk. ASD cases were matched with controls from the source cohort. All procedures were performed blinded to case status. Data regarding disk perimeter, site of cord insertion and disk thickness were extracted from traced photographs of surface (perimeter and cord insertion) and slides (3D depth/thickness) by dedicated algorithms and exported into SPSS 20.0 for analysis. Parametric or nonparametric tests were used, depending on variable distribution, with $p<0.05$ considered significant.

Results: In ASD, placental chorionic surface shape, with **reduced** maximum radius, and **reduced** standard deviation of the radius of the chorionic surface shape were statistically different

from neurodevelopmentally normal controls (each $p<0.05$). There was also a statistically significant **reduced** eccentricity of the umbilical cord insertion In ASD placentas compared to those of normal controls.While mean disk thickness was not different between ASD and controls, there was **reduced** maximum disk thickness and **reduced** standard deviation of disk thickness that was observed subjacent to placental chorionic surface vessels of specific calibers(ech $p<0.05$).

Conclusions: Our findings support a global impression of ASD placentas as being more constrained, less variable in shape, less flexible in growth to permit asymmetry of cord insertion, with more restricted villous branching growth for any given caliber of overlying chorionic surface vessel. The reduced variability is not sufficient to yield an increased rate of fetal growth restriction,t, but may place an at risk fetus at a disadvantage of lesser compensatory capacity and greater vulnerability to gestational stressors including inflammation and/or oxidative stress, gestational exposures that have been associated with ASD risk. Thus, the abnormal placenta we have documented may be a perinatal biomarker and also on the causal pathway to the persistent neuronal injury that has been suggested to underlie ASD.

## 112 Early Biomarkers and Endophenotypes of ASD: From Processes to Prognosis

*Discussant:* T. Insel *National Institute of Mental Health (NIMH)*

*Organizer:* K. Pierce *University of California, San Diego*

Biomarker discovery in medicine is foundational to advancing knowledge and developing beneficial clinical applications. Autism is a strongly genetic disorder, and as such, research on endophenotypes, a special case of biomarkers, is an especially important avenue to identification of genetic factors underlying neural and clinical manifestations. However, biomarker discovery is at an early stage because of the challenges in studying the disorder in the first years of life, its changing phenotypic nature as early development progresses, and its multidimensional genomic, biological and behavioral character. Nonetheless, as presented and discussed in this panel, new research studies using innovative systems biology, imaging and clinical methodologies, have been successful in illuminating genomic and neural developmental bases of the disorder, explicating the neurofunctional bases of important aspects of clinical heterogeneity, identifying endophenotypes and uncovering potential diagnostic and prognostic signatures in at risk infants and toddlers. Discussion will address the pivotal role played by early biomarkers in general and endophenotypes in particular in clarifying mechanisms and processes, phenotypic heterogeneity, neural and clinical developmental trajectories. Discussion will consider early biomarkers as standing at a crucial crossroad pointing backward to earlier developmental processes, states or events, including potential etiological ones, and forward insofar as they explain unfolding development and serve as diagnostic and prognostic risk predictors.

**112.001** Abnormal Visual Attention As Revealed By Eyetracking As an Early Biomarker of ASD. K. Pierce*[1], S. A. Marinero[2], R. Hazin[1], C. Carter[1] and A. Malige[1], (1)*University of California, San Diego*, (2)*UCSD ACE Lab*

Background: Many children with autism appear transfixed by the presence of repetitively moving objects, such as the spinning of a toy car wheel. Our previous study suggested that abnormally heightened attention to geometric repetition might be a biomarker of a particular ASD subgroup, and reported high diagnostic classification accuracy rates (i.e., 99%), based in visual fixation towards geometric images. While results were encouraging, the sample size was small and analyses did not examine traits may be associated with the subgroup of toddlers that strongly fixate on geometric images. This is essential for defining valid endophenotypes that may be useful in future genetic, animal model, and treatment studies. Moreover, comparing gaze patterns in sibling pairs concordant and discordant for ASD might provide clues to the genetic underpinning of this unique subgroup.

Objectives: The objectives were threefold. First, to determine if patterns of eye gaze could be used to accurately classify a toddler as ASD using a large, diverse, sample. Second, to examine the relationship between an ASD toddler ғs preference for geometric images and his/her symptom profile. Third, to examine correlations in fixation patterns between sibling pairs concordant or discordant for ASD.

Methods: 334 toddlers ranging in age between 12-48 months participated. Toddlers were independent from the original study and came from a range of diagnostic categories including ASD (n=115), ASD-Features (n=20), developmental delay (n=57), other issue (e.g., motor delay, n=53), typical (n=64), and typically

developing siblings of an ASD proband (n=25). Toddlers watched a 1-minute movie containing both dynamic geometric and social images and fixation duration within each area of interest and number of saccades were recorded using a wireless eye tracker. Toddlers were diagnostically and psychometrically evaluated with a range of tests including the ADOS and Mullen by an experienced diagnostician.

Results: ASD toddlers demonstrated significantly greater fixation on geometric images than all other diagnostic groups (ASD vs DD, t170=5.05, P<.0001; ASD vs Other, t166=3.23, P=.001; ASD vs TD, t177=6.43, P<.0001; ASD vs TD SIB, t138=5.43, P<.0001), except the ASD Feature Group (ASD vs ASD Features t133=1.3, P=.19). If a toddler fixated on geometric images greater than 69% of the time, the chances of that toddler being accurately diagnostically classified as ASD was 98%. As a group, ASD toddlers that preferred geometric images had lower IQs and greater symptom severity (all p <.001). Concordance rates in eye gaze behavior were significantly correlated in siblings concordant for ASD (ICC=.56, p < .001), but not in other sibling groups (ns).

Conclusions: High diagnostic classification accuracy rates within a large sample suggests that abnormal visual attention to geometric images is a biomarker of a specific type of ASD toddler. Abnormally heightened attention may not only signify ASD risk, but may yield prognostic information as well; ASD toddlers that preferred geometric images had worse cognitive, language, and social skills than other toddlers. Moreover, significant correlations in eye gaze patterns in sibling pairs concordant for ASD suggests that a preference for geometry might signify a genetically driven, specific sub-type of ASD child.

**112.002** Language-related functional neuroimaging biomarkers in autism infants and toddlers with differing language outcome and developmental trajectory. M. V. Lombardo*[1], K. Pierce[2], L. T. Eyler[2], C. Carter[2], C. Ahrens-Barbeau[2], S. Solso[2], K. Campbell[2] and E. Courchesne[2], (1)*University of Cambridge*, (2)*University of California, San Diego*

Background: Early language development is central for parsing phenotypic heterogeneity and predicting later outcome in ASD. However, little evidence exists testing whether atypical neural mechanisms in ASD infants and toddlers underlie such heterogeneity in early language development.

Objectives: To test early behavioral trajectories and neural response to speech in infant/toddler ASD subgroups differentiated on the basis of early childhood language outcome.

Methods: Eighty-four age- and sex-matched 11-47 month olds (60 ASD; 24 TD; mean age = 26.4 months old, SD = 8.7) were scanned with fMRI at UCSD during sleep using the Story Language Paradigm (Redcay & Courchesne, 2008). Development was characterized longitudinally on the Mullen, ADOS, and Vineland over a period of 8-51 months. ASD was split into 3 language outcome subgroups ('poor', 'good', and 'optimal') on the basis of Mullen receptive (RL) and expressive language (EL) T-scores at about 1 year after scanning (ASDPoor: n=24, T<40; ASDGood: n=24, 40≤T<50; ASDOptimal: n=12, T≥50). fMRI data were analyzed with standard pipelines (e.g., AFNI, SPM) with head-motion measures as covariates in all analyses and correction for multiple comparisons at FDR q<0.05.

Results: Group-by-development interactions were observed for EL ($F(3,78)$ = 13.57, $p$ = 3.3 x $10^{-7}$) and RL ($F(3,78)$ = 5.76, $p$ = 0.001). ASDGood, ASDOptimal, and TD toddlers improved with age, while ASDPoor toddlers declined or failed to sustain developmentally appropriate progress. Similar group-by-development interactions were observed across the visual reception subscale of the Mullen and Vineland communication, socialization, and adaptive behavior subscales, but not the ADOS. ASDGood, ASDOptimal and TD toddlers also showed robust bilateral speech-related activation of language-related perisylvian temporo-parietal areas, while ASDPoor toddlers showed little to no activation even at the most liberal uncorrected thresholds (e.g., p<0.05 uncorrected). Group comparisons revealed significantly less activation in ASDPoor compared to all other groups in bilateral language-related temporal cortices, as defined by an independent ROI from a meta-analysis of 553 studies on 'language' from neurosynth.org (LH: $F(3,79)$ = 4.49, $p$ = 0.006; RH: $F(3,79)$ = 2.84, $p$= 0.04) and with whole-brain analyses. ASDGood and ASDOptimal toddlers also showed increased speech-related superior temporal cortex connectivity with frontal cortex, amygdala, and ventral striatum compared to TD. Finally, a

support vector machine classifier made ASDGood vs. ASDPoor predictions solely based on speech-related superior temporal cortex activation patterns with ~70% accuracy (p=0.005) and generalized at similar levels when making predictions for ASDOptimal and TD.

Conclusions: Heterogeneity in early ASD language development is manifest as subgroups with differing early neural organization for language. Hypoactive language-related temporal cortex is specific to ASD toddlers who exhibit very poor early language development and outcome. In contrast, these same language-related temporal cortex regions remain functionally intact and are over-connected with frontal and subcortical areas in ASD toddlers with good or optimal language outcome and improving development. Such differences may be indicative of non-overlapping etiologies (e.g., genetic, molecular/cellular pathways) and/or distinct early developmental processes (e.g., experience-dependent change). This work is also important for further developments in the discovery of early neural biomarkers for early language prognosis in ASD.

**112.003** The use of high density EEG to investigate circuit miswiring in infants at risk for autism. C. A. Nelson*[1], A. R. Levin[1], M. F. Shi[2] and H. Tager-Flusberg[3], (1)*Boston Children's Hospital*, (2)*Harvard College*, (3)*Boston University*

Background: Autism spectrum disorder (ASD) is a complex, highly heritable disorder that involves primary impairments in language and communication. The disorder is heterogeneous and long-term outcomes vary considerably. In large scale studies of infants with an older sibling with the disorder, it has been estimated that approximately 1:5 such infants will eventually be diagnosed with an ASD.

Objectives: A number of investigators have proposed that autism reflects a "connectopathy," in which there is an overabundance of local connections and a shortage of long distance connection. Examining neural circuitry in living children (vs. animals), however, is challenging. Nevertheless, in our work we have made use of advanced signal processing tools to examine the development of neural circuitry.

Methods: As part of our ongoing longitudinal study of high risk infants, task and resting EEG was collected on 208 infants ranging in age from 3 to 36 months of age. EEG was recorded from 128 scalp sites, using EGI sensor nets. Three components of resting EEG were examined. First, EEG coherence was examined as indexed by the mean coherence between all electrode pairs represented in the 10-20 system, with a particular emphasis on the delta and theta bands. Second, alpha rhythm in electrodes over the primary motor cortex was measured, which typically decreases in amplitude when one person observes another performing a motor action, a phenomenon known as mu suppression. Third, coupling between the phase of the theta band pattern and the amplitude of the gamma band pattern was also examined.

Results: EEG coherence results has demonstrated a peak in mean coherence (particularly in the delta and theta bands) at 24 months in children who develop ASD, but at 12 months in children who do not develop ASD. These findings demonstrate that infants with an older sibling with ASD show a corresponding peak in mean coherence in the beta and gamma bands that is not seen in children with a typically developing older sibling. Mu suppression results have shown that at 9 to 18 months, some of the infants who develop ASD show a lack of alpha suppression in primary motor cortex (mean alpha power 20.5 $\mu V^2$ at 9 months and 14.6 $\mu V^2$ at 18 months in high risk infants who develop ASD, versus 6.7 $\mu V^2$ at 9 months and 4.9 $\mu V^2$ at 18 months in high risk infants who do not develop ASD), a phenomenon which has previously been seen in older children and adults with ASD. Finally, coupling analyses have shown increased phase amplitude coupling (PAC) in the temporal regions in infants 3-36 months who develop ASD (Mean modulation index 0.95 left temporal, 0.82 right temporal) compared to those who do not (Mean modulation index 0.21 left temporal ($p = .003$), 0.08 right temporal ($p = .007$).

Conclusions: Preliminary EEG analyses thus far appear promising both as an endophenotype of high ASD risk and as a potential biomarker for ASD diagnosis.

**112.004** Cross-Tissue Gene Networks Distinguish Normal from Abnormal Brain Development in ASD Toddlers. T. Pramparo*[1], K. Campbell[2], C. Carter Barnes[3], S. A. Marinero[4], S. Solso[3], J. Young[3], M. Mayo[3], R. Zablocki[3], A. Dale[5], C. Ahrens-Barbeau[3], S. Murray[5], L. Lopez[3], R. Xu[5], K. Pierce[2] and E. Courchesne[2], (1)*Autism Center of Excellence, UCSD*,

(2)*University of California, San Diego*, (3)*UC San Diego ACE*, (4)*UCSD ACE Lab*, (5)*UC San Diego*

**Background:** Genetic mechanisms underlying early neural maldevelopment in toddlers with ASD remain uncertain, and no genetic or functional genomic signatures exist to detect risk for ASD at early ages.

**Objectives:** To identify functional genomic abnormalities underlying neural development and risk signatures in ASD.

**Methods:** A general population screening approach was used to allow prospective, unbiased recruitment and study of ASD and control (typically developing and mildly language delayed) infants and toddlers from community pediatric clinics. Whole-genome leukocyte expression and MRI-based neuroanatomic measures were analyzed in a sample of 142 males ages 1-4 years. Co-expression and connectivity patterns analyses were performed to identify gene modules and hub-genes associated with variations in neuroanatomic measures. Protein-protein interaction analysis revealed hub-genes physical interactions.

**Results:** Two modules, cell cycle and protein folding networks, were strongly correlated in control toddlers with brain size, cortical surface area, and cerebral gray and white matter. Genes in these modules were found highly expressed in the human brain during first and second trimesters and with reduced expression after birth (BrainSpan). The same two modules were only weakly correlated with neuroanatomic measures in ASD. In control toddlers, modulation of expression in hub-genes with cell cycle functions accounted for smaller to larger brains. Such hub-genes were lost in ASD, and the new set had minimal impact on regulating neuroanatomy. In ASD toddlers with enlarged brains, none of the top ten normal hub-genes were related to brain size measures, and in ASD toddlers with reduced brains, a different set of cell cycle genes impacted size. Unlike controls, ASD toddlers displayed significant correlations with an abnormal array of different gene networks including cell adhesion, immune/inflammation, and translation. A genomic signature enriched in immune/inflammation and translation genes displayed 77% to 82% classification accuracy.

**Conclusions:** The functional genomic pathology underlying variation in early brain development and size in ASD involves disruption of cell cycle and protein folding gene networks, which govern neuron number and synapse formation. Genomic pathology in ASD was present across all developmental brain sizes from small to abnormally large. Importantly, genomic pathology underlying small brain size in ASD differed significantly from the one underlying brain enlargement. Cell cycle abnormalities included changes in expression, connectivity and network membership patterns of hub-genes. ASD genomic pathology also involved the abnormal relationship of cell adhesion, immune/inflammation and translation networks to brain development. Previously, we reported cell cycle gene networks are disrupted in prefrontal cortex in postmortem ASD children. Thus, we hypothesize that prenatal disruption of key developmental gene networks in ASD may lead to known defects of abnormal neuron number, brain and body growth, and synaptic development and function. A candidate gene expression signature of risk for autism in infants and toddlers was identified. Knowledge of genomic pathology and relationships to heterogeneity of early brain growth abnormality in ASD will illuminate the various brain bases of different subtypes of ASD and facilitate discovery of genomic early diagnostic leading to earlier treatment as well as development of targeted biotherapeutics. Brain size and genomic defects are important autism endophenotypes.

## 113 Characterizing Autism: A Re-Examination of the Diangosis and the Phenotype

*Discussant:* I. L. Cohen *New York State Institute for Basic Research in Developmental Disabilities*

*Organizer:* E. B. London *New York State Institute for Basic Research in Developmental Disabilities*

In the 1970's the psychiatric community took a bold step in creating the DSM-3, which for the first time provided standardized and reliable criteria for psychiatric diagnoses. Despite being an important improvement, it also created new problems. The diagnoses were created by consensus of committees rather than from data-driven evidence to ensure external validity. The framers warned that these diagnoses were "way stations" until better scientifically-based diagnoses could be made. Categories had unclear boundaries with other disorders and with normality. These categories, (which did not "carve nature at its joints"), created the new concept of co-morbidities. It is the rare patient who has only one diagnosis.

The categorical diagnoses are poor at prognosis and treatment guidance and have a wide range of heterogeneity in their presentations. Despite these problems, the diagnoses have been reified and the failure to use these categories imposes severe restrictions and often skews the research that is done. In this symposium we intend to examine the diagnosis of DSM autism in light of the problems enumerated above, using evidence from clinical, genetic and brain circuit studies. We also will review some of the proposed alternatives to the categorical diagnoses, with special attention to the NIMH's RDoCs.

**113.001** How Can Genetic Research Inform Current Psychiatric Diagnostic Practice?. S. L. Santangelo*, *Maine Medical Center/Maine Med Ctr Research Institute*

Background:

In February 2013, the cross-disorder group (CDG) of the Psychiatric Genomics Consortium (PGC), published the largest genetic study of mental illness ever done. Scanning the genomes of over 33,000 patients and nearly 28,000 controls, we investigated the possibility that common genetic variants might affect susceptibility to five psychiatric disorders, including autism, ADHD, major depressive disorder, bipolar disorder and schizophrenia. We identified four common genetic risk loci with significant association to all five diseases, including SNPs in two calcium channel genes that regulate the flow of calcium in brain cells. We also found that there were some variants shared by some but not all of the disorders. In August 2013, the CDG/PGC published a second paper that applied quantitative genetic methods to examine the relationships between the five disorders and found substantial evidence for shared genetic etiology among them. These findings raise the questions of how unique and separable these five disorders are and what the relative strengths of unique and shared pathophysiologies might be across the disorders.

Objectives:

This talk will describe how the results of large-scale genomic studies can be used to inform psychiatric nosology, with particular attention to the diagnosis of DSM-V autism/autism spectrum disorder.

Methods:

Evidence will be reviewed from genome-wide association studies of psychiatric diagnostic categories, such as the ones cited above, as well as studies of quantitative phenotypes, using various molecular and statistical methods.

Results: N/A

Conclusions:

The genetic studies reviewed provide empirical evidence that genetics/genomics can help us move beyond the design of psychiatric nosological systems based on purely descriptive clinical categories to those informed by biological factors in disease causation. Further, genetic and genomic studies can contribute to the prediction, prevention and treatment of psychiatric diseases such as autism and to the identification of molecular targets for new generations of psychotropic drugs, some of which are likely to cross arbitrarily assigned disease classification boundaries.

**113.002** Brain Circuits and Functions Across Psychiatric Disorders. J. A. Sweeney*, *Center for Autism and Developmental Disabilities, UT Southwestern Medical Center*

Background: Common psychiatric disorders as we now define them are not discrete diseases with specific pathophysiology, but rather broad heterogeneous syndromes with multiple overlaps in their genetics, neural system involvement and behavioral features. Meaningful subgroups within broad syndromes have been repeatedly hard to identify using behavioral and symptom data. This situation complicates efforts to define pathophysiological mechanisms, it slows treatment development, and it adds uncertainty and instability to clinical diagnostic practice. The long experience with these challenges in adult psychiatric disorders is now being recapitulated autism spectrum disorders, and that extensive history can inform expectations and strategies for addressing these challenges now being encountered in ASD after its boundaries were expanded.

Objectives: Data from the BSNIP deep phenotyping project will be reviewed to show how issues of diagnostic boundaries have been examined in psychotic disorders. The overlap of affective and nonaffective psychotic disorders in symptom, imaging and cognition data shows how a dimensional model across disorders can offer some advantages to categorical approaches. The neural circuitry impaired in psychotic disorders

also has parallels as well as differences from those we have observed in ASD, and these will be discussed to illustrate the scale of overlap of ASD with other neuropsychiatric disorders.

Methods: The BSNIP study involved clinical, imaging, electrophysiological and neurocognitive studies with over 2000 participants (probands, family members and controls). Cognitive and imaging studies of ASD (n=100) will be presented and compared to findings with psychotic disorder patients.

Results: Similarities and differences observed across psychotic disorders will be presented. Some measures seem to fit dimensional models across psychotic disorders, while some deficits are more disorder specific, suggesting that dimensional and categorical diagnostic approaches both have value. Overlaps and differences from ASD data will be presented.

Conclusions: The history of diagnostic practice in heterogeneous/complex neuropsychiatric syndromes has many examples of both overlap across syndromes and difficulty defining discrete subgroups within the syndromes. Resolving heterogeneity using molecular and systems biology approaches and dense phenotyping offer promising strategies for addressing this challenge. There are several reasons why success may be easier in ASD than in other common neuropsychiatric disorders.

**113.003** The Rdoc and Autism Research. A. Wagner*, *NIH/NIMH*

Background:

The NIMH- initiated the Research Domain Criteria (RDoC) is an attempt to develop a framework to study mechanisms of mental disorders that cut across traditional boundaries of mental disorders, with the goal of facilitating research that aligns with genetics, other areas of neuroscience and behavioral science. Many investigators have questions about the implications of the RDoC initiative for NIMH priorities, and whether there is an inherent conflict between RDoC classification and other psychiatric diagnostic entities such as the DSM-5.

Objectives: To demonstrate the potential application of RDoC-relevant research in ASD, recent research findings from the autism field that fit the "spirit" of RDoC will be presented.

Methods: The method for the development of RDoC incorporates input from the scientific community, and is envisioned as an ongoing, iterative process. This presentation will review the RDoC goals, the process of its development, and its role in ASD research. There will be opportunities for discussion and questions from participants.

Results: The ultimate goal of RDoC is to provide a foundation that can lead to more effective diagnosis, the identification of more homogeneous targets for interventions, and the development of new treatments or more precise matching of treatments to patients.

Conclusions:

Workshop participants will have a better understanding of NIMH goals with the development of RDoC and how this approach aligns with autism research.

**113.004** The Autism Diagnosis: Ongoing and Unadressed Problems. E. London*, *NYS Institute for Basic Research in Developmental Disabilities*

Background:

Kanner published his original paper Disturbances of Affective Contact in 1943. In 1944 he named this disorder as early infantile autism. Using Kanner's own description, "almost overnight, the country seemed to be populated by a multitude of autistic children". "Many authors began to dilute the original concept of infantile autism by diagnosing it in many disparate conditions which show one or another isolated symptom found as a part feature of the overall syndrome". While the majority of Europeans were satisfied with a sharp delineation of infantile autism as an illness *sui generis*, (of its own kind or a natural kind) there was a tendency in America to view it as a developmental anomaly ascribed exclusively to maternal emotional determinants. In the 1970's the DSM-3 was published which institutionalized categorical diagnosis of all psychiatric disorders, thus supporting the assumption that these were illnesses su generis. Few today associate autism with maternal emotional determinants; however the basic questions remains; is autism a disorder sui generis or is it just a syndrome which merges into the rest of developmental disorders and other psychiatric disorders.

Objectives:

In this talk I will review the overlap of autism with other psychiatric and neurologic disorders and discuss the centrality of these findings; review the problem of co-morbidities; review the problem of reification of diagnosis and how that affects both clinical practice as well as phenotypic decisions for research; and review the effect that a re-organization of diagnostic concepts might have on the major stakeholders which includes primary care physicians, psychiatrists, behaviorists, educators, researchers, policy makers and affected individuals and their families.

Methods: N/A

Results:

I will present evidence that the categorical diagnosis of autism has flaws which have far reaching effects on clinical and research practice. In its stead I propose that we view autism as one outcome of anomalous brain development. Rather than seeing co-existing problems as co-morbidities with the implication of there being two or more potentially unrelated disorders, each sign or symptoms deserves equal weight in characterizing the clinical entity which a given individual may have. Without a preconceived notion of which symptoms are "core" symptoms we have the scientific freedom to explore other pathopysiololgic models. An example might be the recent findings by several groups that in very young children, motor deficits were the most predictive of later development of autism, despite these symptoms having a small or peripheral role in the diagnosis.

Conclusions:

In order to harmonize both the clinical and the research nosology, I propose that those with autism be part of a "super diagnostic group" which could be termed "Developmental Brain Disorders". This could be followed by a second axis in which the specific findings of that individual could be listed. This is closer to the model currently used by the ICD for medical diagnoses.

## 114 Autism in Africa

*Discussant:* P. de Vries *University of Cape Town*

*Organizer:* R. A. Hoekstra *The Open University*

There is a dearth of autism research on the African continent; this scientific panel session aims to highlight recent research progress addressing this gap. The panel includes scientific presentations from two sub-Saharan African countries, using a combination of qualitative and quantitative methodologies and reporting on both urban and rural African populations. Altogether, the findings from these studies highlight the major barriers to appropriate support for families of children with autism in Africa (including the severe shortage of diagnostic and educational services, lack of awareness about autism and its causes, and high levels of stigma), and report on a promising scalable model that can help tackle these problems by training frontline community-based health extension workers. The challenges and opportunities discussed in these presentations apply not just to the countries under study, but have relevance for the entire African continent and low/middle income countries elsewhere. During the panel discussion these common themes will be reviewed and priority areas for future research and opportunities for intervention will be highlighted, in order to facilitate future autism research, advocacy and capacity building efforts.

**114.001** Services for Children with Autism and Their Families in Ethiopia: Service Providers' Perspectives. B. Tekola Gebru*[1], Y. Baheretibeb[2], I. Roth[1], D. Tilahun[2], A. Fekadu[2], C. Hanlon[3] and R. A. Hoekstra[1], (1)*The Open University*, (2)*Addis Ababa University*, (3)*King's College London*

Background: Knowledge about autism in general, and service provision to children with autism and their families in particular, is extremely limited in Africa; there are no previous studies on autism in the horn of Africa (Elsabbagh et al., 2012). In Ethiopia, the prevalence of autism is unknown, but prevalence studies of general mental health problems and intellectual disabilities indicate that these problems are at least as prevalent as in high-income countries (WHO, 2008).

Objectives: To describe the current service provision for children with autism and their families in Ethiopia in order to assist advocacy for improved services and to inform development of future service interventions.

Methods: Audiotaped semi-structured qualitative interviews were conducted with all 10 service providers (n=10) for children with autism and their families in Ethiopia. Data were analysed using thematic analysis.

Results: Services for children with autism and their families are centralised in the capital city.

There are four types of service providers: 1) two psychiatric clinics in government-run hospitals and a private clinic, 2) two centres run by parents of children with autism, 3) one government and two private schools which have inclusive education programmes for children with autism and 4) two community-based organisations. Autism diagnoses, in the minority of cases where these are available, are made in the psychiatric clinics, based on a clinical interview and observation following DSM-IV criteria. There are no standardised diagnostic instruments. The scope of Ethiopian service providers tends to be broader than typically seen in high-income countries, with the parent-run centres and community-based organisations also providing some informal diagnoses. Access to centres run by parents of children with autism is mostly restricted to well-educated and more affluent families; these centres also have long waiting lists. There are no diagnostic or educational services in the rural areas, where 85% of the population lives. In these areas autism usually remains undetected because of limited health care, low levels of awareness and stigma. Autism type symptoms are often seen as a punishment for wrongdoing from supernatural forces. Several interviewees said that parents hide children with such problems away from the community. Children with autism and their families experience social exclusion and negative attitudes/judgements from others. Awareness about autism among the general public and health professionals has increased recently mainly thanks to the efforts of centres run by parents. In recent years, they have organised a mass walk, fundraising events and conferences; given media interviews; produced documentary films and wrote newspaper articles.

Conclusions: Although knowledge about autism has improved in recent years, autism in Ethiopia is still surrounded by lack of awareness and stigma. There is a severe lack of diagnostic and educational services for individuals with autism and their families; facilities are non-existent in rural areas. Apart from a need for increase in service provision there is a clear need for culturally and contextually appropriate autism diagnostic instruments.

**114.002** Perceived Causes of Autism in Rural and Urban Multi-Cultural Context on the Kenyan Coast. J. K. Gona*[1], C. R. Newton[1], K. Rimba[1], R. Mapenzi[1], M. Kihara[2] and A. Abubakar[3], (1)*Kenya Medical Research Institute*, (2)*United States International University-Africa*, (3)*Utrecht University*

Background: Different cultures have different beliefs on perceived causes of autism. Cultural values and beliefs on perceived causes of autism may determine which treatment families will accept or reject. The role of religion in multi-cultural settings also offers a major basis of support for families of children with autism. Autism studies in rural and urban settings within a multi-cultural context investigating perceived causes of autism have not been conducted in Kenya. This study interviewed participants from rural and urban settings with different religious persuasions from the coastal region of Kenya to establish perceived causes of autism.

Objectives: (a) to determine perceived causes of autism in a multi-cultural context; (b) to establish whether religion influences the way people perceive causes of autism.

Methods: We recruited a total of 104 participants consisting of parents of children with and without autism, teachers, clinicians, social workers and project managers from different ethnic and religious backgrounds living in rural and urban settings on the Kenyan Coast. Interviews and focus group discussions were the methods of data collection. The interviews and the focus group discussions were recorded, transcribed and translated into English; and imported to the NVIVO 7 program for storage and management. Content analysis was utilized to analyze the data. The text was read thrice for familiarization to identify key issues. The data were coded using free nodes to identify consistencies and differences. All the free nodes with similar messages were grouped into tree nodes each bearing a name of a theme. Connections within and between themes were identified for interpretation.

Results: Cultural beliefs in evil spirits, witchcraft and curse were viewed to cause autism by participants from both rural and urban settings. In addition, biomedical causes such as brain insults, malnutrition, misuse of drugs and perinatal complications were stated. The potential role of genetic influences was also cited. There were no indications of religious influences on perceived causes of autism

Conclusions: The results revealed that participants held similar views despite coming from different settings with cultural and religious diversity. Knowledge on perceived causes of autism and its impact on treatment of autism may provide valuable conceptual understanding for health and education practitioners working with parents of children with autism in these settings.

**114.003** Increasing Autism Awareness Among Rural Community-Based Health Extension Workers in Ethiopia: The Health Education and Training+ (HEAT+) Project. R. A. Hoekstra*[1], B. Tekola Gebru[1], D. Tilahun[2], A. Fekadu[2], Y. Baheretibeb[2], I. Roth[1], B. Davey[1] and C. Hanlon[3], (1)*The Open University*, (2)*Addis Ababa University*, (3)*King's College London*

Background: In rural Ethiopia basic health services are provided by 39,000 community-based health extension workers (HEWs) serving a population of 73 million. Most HEWs only received basic health training not encompassing mental health. Recently a first cohort of HEWs upgraded their training using the Health Education And Training (HEAT) programme developed by The Open University UK in collaboration with the Ethiopian Federal Ministry of Health (FMoH), UNICEF and AMREF. HEAT provided HEWs with training in mental health and childhood developmental problems for the first time, although specific autism training was limited.

Objectives: i) Compare knowledge regarding autism and general mental health in HEWs who completed HEAT training and HEWs who were not yet trained; ii) identify remaining gaps in the knowledge of HEAT-trained HEWs.

Methods: Participants included 108 HEWs who had recently completed the HEAT upgrading programme and 266 HEWs who were not yet trained. All HEWs were female; both groups had similar age (mean 25.78 vs. 25.82 years), work experience length (mean 74 vs. 70 months) and distribution of religious affiliations. Both groups completed a survey including an autism case vignette, followed by questions on autism characteristics, its causes and possible treatments (adapted from the Autism Survey; Stone, 1987). The survey also asked general feedback on the HEAT materials (from those already trained) and the importance of mental health and childhood developmental problems.

Results: HEAT-trained HEWs were less likely than non-trained HEWs to attribute autism to a curse, to think that autism is contagious, can be cured by spiritual or traditional treatments, or that autism symptoms can improve by beating the child (all $p<.01$). However, the majority of HEWs in both groups thought children with autism are deliberately disobedient (69% vs. 75%; $p>.05$) and that autism can be caused by unloving parents (72% vs. 69%; $p>.05$). HEAT-trained participants were more likely to regard mental health ($p=.003$) and childhood developmental problems ($p=.007$) as very important. The majority (69%) of HEAT-trained HEWs indicated that they apply the training at least once a month in their job; since finishing the training 36% of them had organised one or more mental health awareness raising meetings in their community. Yet, most (74%) HEAT-trained participants indicated they would like more training on childhood developmental disorders.

Conclusions: HEAT-trained HEWs were less likely to have incorrect beliefs about the causes and treatment of autism and were more aware of the importance of mental health and childhood developmental disorders. However, there were also important gaps in their knowledge and participants indicated they would benefit from more training. Following these findings our team produced five videos teaching HEWs how to interview mothers of children with autism or intellectual disability, in order to improve early detection, supportive counselling and problem solving. Additionally, a 'Mental Health Pocket Guide' was produced, endorsed by the FMoH, with dedicated sections on autism and intellectual disability. The effectiveness of these enhanced training materials will be evaluated in a follow-up assessment. All training materials are freely available, allowing for the HEAT model to be applied elsewhere.

**114.004** Comparing Beliefs, Attitudes and Social Distance of Community Health Extension Workers Towards Children with Autism in Ethiopia: Impact of Brief Training through the Health Education and Training (HEAT) Programme. D. Tilahun*[1], C. Hanlon[2], B. Tekola Gebru[3], A. Fekadu[1], Y. Baheretibeb[1], I. Roth[3], B. Davey[3] and R. A. Hoekstra[3], (1)*Addis Ababa University*, (2)*King's College London*, (3)*The Open University*

Background: Improving access to health care for people with autism in Ethiopia is highly dependent on the awareness and attitudes of frontline community-based health extension workers (HEWs). The Ethiopian Federal Ministry of Health

is upgrading the skills of HEWs through the Health Education And Training (HEAT) programme in collaboration with The Open University UK, AMREF and UNICEF. HEAT includes a brief overview of child mental health and developmental disorders.

Objectives: To compare beliefs and attitudes towards, and preferred level of social distance from, children with autism in HEWs who have and have not received HEAT training.

Methods: HEWs were selected randomly from two groups: (i) those who had received HEAT mental health training and (ii) those not trained. Beliefs, attitudes and preferred social distance in relation to children with autism were measured using questions from the World Psychiatric Association Stigma Toolkit. Social distance refers to the level of distance favoured by one societal group towards another.

Results: A total of 374 HEWs were included in the analyses, 108 had received HEAT training and 266 had not been trained. Across both groups of HEWs, stigmatising beliefs and attitudes were high. HEWs who had been trained in HEAT were less likely to endorse positive outcomes for children with autism, for example, that they could play with other children, make their parents proud or get married. The trained HEWs were also more likely to consider people with autism to be a public nuisance and did not differ from the untrained HEWs in their endorsement of other negative stereotypes such as dangerousness.

Despite these stigmatising beliefs, HEWs with HEAT training were less likely to favour social distance from children with autism and their families. After adjusting for age, educational level and religious affiliation, HEWs with HEAT training were less likely to be afraid to have a conversation with a child with autism (adjusted odds ratio (aOR): 0.52 (95% confidence interval (CI) 0.31, 0.86)), to report that they would not be able to maintain a friendship with the parent of a child with autism (aOR 0.57; 95%CI 0.33, 1.00) or to be ashamed to be seen out in the street taking care of a child with autism (aOR 0.22; 95%CI 0.06, 0.73). None of the trained HEWs supported chaining up children with autism, compared to 4.5% of non-trained HEWs.

Conclusions: Even brief training was associated with a decreased tendency, by HEWs, to favour social distance towards children with autism. This is likely to have an important positive impact on HEWs' willingness to provide care. However, training did not lead to more positive beliefs about outcomes for children with autism. In this rural Ethiopian context those children with autism who are recognised by HEWs are likely to be severely affected. As the HEWs gain an initial awareness of autism through training they may, therefore, begin to reflect on the associated problems. This may explain the apparent paradox of increased negative expectations. Future HEW training may benefit from increased focus on the potential positive outcomes of autism.

## 115 Cognitive Modulation of Arousal in ASD: Linking Emotion Processing and Anxiety Across Development

*Discussant:* V. Slonims *Guy's and St Thomas' NHS Foundation Trust*

*Organizer:* E. J. Jones *Birkbeck College, University of London*

Many individuals with ASD struggle to understand emotions and experience clinically significant anxiety, but little is known about the developmental origins of these difficulties. Here, we present data suggesting that both problems stem from atypical integration of cognitive and arousal responses to emotional situations. During development, infants learn to make appropriate cognitive interpretations of arousal states through social interaction. In ASD, we propose that early delays in face processing and atypical arousal responses compromise this developmental process, leading to persistent problems with emotional understanding and anxiety. Specifically, Jones and Wagner show that atypicalities in cognitive and arousal responses to emotion faces are present in infants at high-risk for ASD, that these atypicalities jointly relate to temperamental fear, and to later social-communicative deficits and early autism classification. Webb shows that children with ASD who display atypical electrophysiological responses to emotion faces at age 3 may be at risk for clinically significant anxiety by age 15. Finally, Gaigg demonstrates that anxiety and emotion understanding are strongly related in adults with ASD, and are underpinned by difficulties in cognitive appraisal of own arousal state. Taken together, these talks support a common developmental route to emotion processing difficulties and anxiety in ASD.

**115.001** Facial Emotions Elicit Atypical Arousal and Visual Attention Patterns in 14-Month-Old Infants at High Risk for Autism. E. J. Jones*[1], T. Gliga[1], S. Rigato[2], T. Charman[3], M. H. Johnson[1] and .. The BASIS Team[1], (1)*Birkbeck College, University of London*, (2)*University of Essex*, (3)*King's College London*

Background:

Many individuals with autism have difficulty understanding emotions in themselves and others (Nuske et al., 2013). Further, many individuals with autism experience clinically significant levels of anxiety (White et al., 2009). However, little is known about the developmental roots of these difficulties. In early development, combining information about arousal state with social signals from caregivers is central to learning to regulate and understand emotions (e.g. Thompson, 2011). In autism, early atypicalities in face processing or in arousal responses to emotional situations could thus compromise this critical developmental process. Here, we test this model by examining visual attention and arousal responses to emotion faces in a group of infants with older siblings with autism. In the chosen paradigm, infants viewed faces displaying emotional expressions (happy, fearful, sad, angry) with direct or averted gaze. This paradigm was chosen because typically developing infants show robust preferences for happy faces with direct gaze, and fearful faces with averted gaze (Rigato et al., 2013). Atypicalities may indicate a diminished ability to interpret the communicative intent of facial expressions.

Objectives:

To examine whether infants at high risk for autism display atypical gaze and arousal responses to facial emotion, and whether atypicalities are linked to high levels of temperamental fear.

Methods:

Participants were infants with older siblings with autism (n=56) or typical development (n=25) tested at 8- and 14-months. Gaze was recorded with TOBII eye-tracking technology and processed using Matlab. Key dependent variables include first look direction and pupil dilation responses during each slide.

Results:

There were no group differences at 8 months. At 14 months, low-risk infants showed the expected pattern of modulation of emotion processing by gaze direction. High-risk infants showed typical (though attenuated) preferences for happy faces with direct gaze; this indicates that they were able to discriminate direct and averted gaze. However, whilst low-risk infants showed very strong preferences for fear faces with averted gaze, high-risk infants showed no significant preferences in this condition. Analysis of pupil dilation indicated that the low-risk group showed greater arousal to faces displaying approach emotions (happy, angry) whilst the high-risk group showed greater arousal to faces displaying avoidance emotions (fear, sad). Finally, the high-risk group showed significantly greater levels of temperamental fear. Within the high-risk group, showing high levels of temperamental fear was associated with an atypical combination of arousal and visual attention responses.

Conclusions:

Taken together, these data suggests that infants at high risk for autism show atypical visual attention to fearful faces; show atypically high levels of arousal in response to fearful and sad faces; and show particularly high levels of temperamental fear that were associated with an atypical combination of visual attention and arousal responses. This is consistent with the proposal that atypical cognitive and arousal responses to emotion faces are present in infants at high risk for autism, and may be related to early behavioral manifestations of increased anxiety. Follow-up of this cohort is ongoing; further analyses will examine the relation between these early atypicalities and symptoms of autism at 24 months.

**115.002** Increased Pupil Size to Emotional Faces in Infants at High Risk for Autism As an Early Predictor of Atypical Development. J. B. Wagner*[1], R. J. Luyster[2], H. Tager-Flusberg[3] and C. A. Nelson[2], (1)*College of Staten Island, CUNY*, (2)*Boston Children's Hospital*, (3)*Boston University*

Background:

Past work with individuals with ASD has found differences in both visual attention and autonomic measures of face processing, including reduced time on core features and heightened sympathetic arousal to faces. Prospective work with infant siblings of children with ASD, a group with as high as a 1 in 5 chance of also developing the disorder, provides an opportunity to look for early markers of atypical face processing, some of which might be predictive of later ASD outcome or other developmental difficulties.

Objectives:

To understand the origins of face processing differences in individuals with ASD, visual scanning and pupil diameter, a measure of sympathetic arousal, were examined in response to emotionally-salient faces in infant siblings of children with ASD. These measures were then examined alongside 18-month social-communicative outcomes and ASD classification to look for early markers that might predict atypical development.

Methods:

At 9-months-old, 38 infants at high risk for ASD (HRA) and 30 low-risk controls (LRC) were presented with static images of fearful, happy, and neutral faces. Each face was presented twice for 10 seconds. A Tobii eye-tracker captured visual attention and pupil size while infants viewed each face.

A set of longitudinal analyses followed HRA and LRC infants through 18 months to ask whether any features of attention and arousal might relate to later outcomes in these infants, as measured by the Communicative and Symbolic Behavior Scales (CSBS) and the Autism Diagnostic Observation Schedule (ADOS).

Results:

Analyses of visual attention to the three emotional faces (both for overall time on faces and for proportion of time on eyes vs. mouth) revealed no influence of group on scanning patterns for LRC and HRA. Analysis of pupil size revealed a significant difference between LRC and HRA, with greater pupil size in HRA than LRC ($p$= .042), suggesting that HRA infants show increased arousal to the emotionally-salient stimuli.

A set of correlations examined 9-month-old attention and arousal to faces and social-communicative behavior at 18 months as measured by the CSBS. In LRC, significantly greater attention to eyes at 9 months was related to higher CSBS social scores at both 12 and 18 months ($r$s > .51, $p$s < .03). In HRA, there was no relation between attention to eyes and later CSBS scores; however, larger pupil size at 9 months was significantly correlated with worse overall CSBS outcomes at 18 months ($r$ = -.44, $p$ = .028). A preliminary set of analyses also examined ASD classification at 18 months and found that the group difference at 9 months for pupil size between HRA and LRC was driven by the subset of HRA infants (N=9) who received a positive 18-month ADOS classification ($p$= .027).

Conclusions:

Taken together, the CSBS and ADOS relations to pupil size in HRA suggest the importance of studying early arousal mechanisms as predictors of later developmental difficulties in ASD and the broader autism phenotype, particularly in the context of emotionally-salient stimuli, as is the focus of the present scientific panel.

**115.003** A Longitudinal Study of Emotion Processing in ASD and the Relation with Other Clinical Symptoms: The Cpea Early Development Study of Autism. K. M. Burner*[1], L. J. Sterling[2], J. Munson[3], A. M. Estes[3], G. Dawson[4] and S. J. Webb[3], (1)*Seattle Children's Hospital*, (2)*UCLA Semel Institute for Neuroscience & Human Behavior*, (3)*University of Washington*, (4)*Duke University Medical Center*

Background: Behavioral and psychophysiological research suggests that emotion processing is impaired in individuals with autism spectrum disorder (ASD). Underlying neural abnormalities in emotion processing may contribute to the variability in social-emotion functioning in children with autism and negatively influence social interactions and the maintenance of social relationships. However, conditions associated with autism such as anxiety and depression are known to influence emotional processing and hyperarousal to emotional stimuli has been proposed as a risk marker for later elevated symptoms in these domains.

Objectives: N/A.

Methods: Participant groups included children who met criteria for ASD at 3-4 years of age and controls (children with neurotypical development and children with developmental delay). Participants were followed longitudinally at age 3, 6, 9 and 15 years of age in the CPEA Early Development Study. Electrophysiological data (using a high density EEG array) was collected during processing of fearful faces and a control face stimulus (neutral or happy faces) at 3, 6 and 9 years of age. Diagnostic, Cognitive, and Face Memory data was available for time points 3-9 years and parent report of internalizing symptoms (via CBCL) was available at 9 and 15 years.

Results: Using event-related potentials, at 3-4 years of age, children with ASD demonstrated delays in fear processing that are related to social ability, including social orienting, and response to distress. Delays in processing speed were also found at 6 years of age. However, by 9 years of age, as a group, the children with ASD did not differ in their responses to fear faces, neither in amplitude nor speed of the ERP components. Responses at 9 were related to internalizing symptoms, with increased amplitude responses correlated with higher scores. By 15 years, the ASD group reported higher levels of internalizing symptoms. Discussion will focus on both group trajectories in fear processing and later ASD and internalizing symptom levels. The role of early hyper- or hypo-processing of fear may be a risk factor for less optimal outcomes.

Conclusions: The CPEA Early Development longitudinal Study provides an opportunity for examining very early processing of fear stimuli, assessed through event – related potentials, in children with ASD and control groups embedded in a rich background of information about diagnostic, cognitive and psychological functioning. This work suggests that early emotion processing vulnerabilities in children with ASD play a role in later social communicative outcomes but also may be related to the susceptibility for internalizing disorders. Understanding how basic processing of fear is related to larger social constructs may inform our understanding of mechanisms that contribute to the heterogeneity in functioning.

**115.004** Alexithymia in Autism: Psychophysiological Correlates and a Possible Route to Anxiety. S. B. Gaigg*[1], G. Bird[2] and D. M. Bowler[1], (1)*City University London*, (2)*Kings College London*

*Background:* Autism Spectrum Disorder (ASD) is frequently associated with Alexithymia, which is characterised by difficulties in identifying and describing one's own emotions (Hill et al., 2004). These difficulties have been shown to account for the problems individuals with ASD often experience in recognising and identifying emotional expressions in others (Cook et al., 2013) and there are reasons to believe that Alexithymia may also lie at the root of the high prevalence of Anxiety in ASD. A major challenge for research on Alexithymia, however, remains that the neurocognitive basis of the phenomenon remains poorly understood and that the construct is measured exclusively through self-report questionnaire measures. In the context of ASD, this hinders the formulation of accounts that specify the neurocognitive mechanisms that lie at the root of the close association between difficulties in emotion recognition, Alexithymia and Anxiety.

*Objectives:* To examine the psychophysiological basis of Alexithymia in ASD and to explore possible associations between Anxiety and Alexithymia.

*Methods:* In *experiment 1* seventy-six adults (33 ASD; 43 TD) completed standardised Alexithymia questionnaires (BVAQ & TAS-20) as well as the Becks Anxiety Inventory (BAI). In *experiment 2*, 13 ASD and 13 TD participants were asked to rate a series of images that ranged widely in emotional salience (valence and arousal) while their Skin Conductance Responses were measured. These smaller groups were carefully selected to match as closely as possible in terms of age, IQ as well as Alexithymia whilst ensuring that Alexithymia scores varied sufficiently to allow for meaningful correlation analyses.

*Results:* In Experiment 1, ASD participants were more Alexithymic on both the BVAQ ($p<.05$) and TAS-20 ($p<.001$) and the two measures correlated significantly with one another for both ASD ($r = 0.42$) and TD ($r = 0.45$) participants. Although groups did not differ on the BAI, Anxiety and TAS-20 correlated significantly in ASD ($r = .52$) but not TD ($r = .19$) participants. In Experiment 2 subjective ratings of arousal were significantly correlated with participant's GSR responses, again in both ASD ($r = .51$) and TD ($r = .55$) groups. By computing correlation coefficients for this association for each individual, we were able to ask to what extent the degree of coupling between subjective and psychophysiological emotional responses is in turn associated with participants' Alexithymia and Anxiety. In both groups, reduced coupling was associated with greater Alexithymia ($r < -0.54$) and increased coupling with greater Anxiety ($r > 0.46$)

*Conclusions*: Our date reveal a complex pattern of associations between Alexithymia, Anxiety and the interplay between subjective and psychophysiological facets of emotional experiences that seem to suggest that

abnormalities in conscious awareness of one's state of arousal contribute to Anxiety as well as Alexithymia in ASD.

## 116 Keynote Address - Lifetime Achievement Awardee

Keynote Address - Lifetime Achievement Awardee

Lifetime Achievement Award. F. R. R. Volkmar*, *Yale University*

## 117 Brain Function

**117.001 1** Brain Metabolites and Behavior in Autism: A Twins Study. S. W. Berquist*[1], M. Gu[1], D. Spielman[1], S. Patnaik[1], S. Cleveland[1], M. Tatavarthy[1], M. Y. Lum[1], J. Hallmayer[1], L. Lazzeroni[1], T. W. Frazier[2], J. M. Phillips[1], A. L. Reiss[1] and A. Y. Hardan[1], (1)*Stanford University School of Medicine*, (2)*Cleveland Clinic Children's Hospital*

Background: Using proton magnetic resonance spectroscopy (1H MRS) to examine a variety of brain metabolites in twins provides an opportunity to assess the contributions of genetic inheritance, disease state, as well as confounding factors while controlling for metabolite variability in the population. The present ongoing study looks to elucidate relationships between 1H MRS metabolite levels and clinical features across a cohort of same-sex twin pairs with autism and high variability in disease severity.

Objectives: 1) To explore differences and similarities among different brain metabolites in MZ and DZ twins, where at least one sibling serves as a proband with autism, and 2) To evaluate the relationship between clinical features and reliably calculated metabolite levels.

Methods: The study aims to recruit 120 same-sex twin pairs, 80 with at least one pair with autism, 40 monozygotic (MZ) and 40 dizygotic (DZ), and 40 typically developing twin pair controls, 20 MZ and 20 DZ. High- resolution MRI and 1H MRS imaging scans are being obtained from all participants. Behavior and cognition are also being assessed to provide specific covariates for neuroimaging variables.

Results: In this preliminary examination, data from 45 twin pairs were analyzed (age range: 6-15 yrs; Mean 11.04 years ± SD 3.23). Correlations between clinical measures of social abilities and repetitive/restricted behaviors and differences in N Acetyl Aspartate/Creatine levels between twin pairs were examined and several associations were observed including relationships in caudate and putamen with measures of rigidity/restricted behaviors and social cognition, respectively. Among the present findings, our investigation has found lower levels of NAA correlated with symptoms such as repetitive behaviors (Left Putamen NAA/Cre vs total RBS-R score, 95% CI -0.001 : -0.03), sensory abnormalities (Left Caudate NAA/Cre vs SPQ total, 95% CI -0.001 : -0.03), affect recognition (Right Putamen NAA/Cre vs NEPSY AR raw score, 95% CI 0.02 : 0.41), and social responsiveness (Right Thalamus GCP+PCh/Cre vs SRS raw score, 95% CI 0.01 : 0.98).

Conclusions: Findings from this preliminary analysis indicate a relationship in autism between brain metabolites and behavior. These observations appear to be consistent with previous reports. Further analyses including more twin pairs will help further current knowledge metabolite abnormalities and neuroanatomic pathways implicated in autism.

**117.002 2** Social Engagement Does Not Modulate Object Processing in Young Children with Autism Spectrum Disorder (ASD): An Electrophysiological Investigation. E. Baker*[1], C. Harrop[1], L. M. Elder[2], K. Abood[1], A. Soares[1] and S. S. Jeste[3], (1)*UCLA Center for Autism Research and Treatment*, (2)*Autism Speaks*, (3)*UCLA*

Background: Many studies have demonstrated that typically developing infants and children learn more successfully when information is presented in a social context, with learning defined as the differential response to stimuli based on their social presentation. This learning can be quantified through a neural response to stimuli using event related electrophysiology (EEG). Because impairment in social interaction represents a core deficit in children with autism spectrum disorders (ASD), we were interested in understanding the effect of social interaction on information processing of this population.

Objectives: We used a novel EEG paradigm that couples a live interaction exposure, in which children are exposed to toys in both a social and non-social context, with an EEG test phase in which these objects presented socially or non-socially are then presented passively. Our aims were to understand the effect of social interaction on information processing in children with ASD by examining the association of the child's social behavior toward the examiner with electrophysiological markers of learning. We hypothesized that children with ASD would demonstrate less engagement during the

interactive exposure phase and, therefore, would not demonstrate a differential response to objects based on their social saliency.

Methods: In the exposure phase, children (2-6 years old) were presented with toys by an adult examiner in either a social or non-social manner. Child and examiner behaviors were coded per trial using both likert scales and quantifiable measures of sociability and level of interaction. In the test phase, children viewed discrete images of the toys while high-density EEG was recorded. EEG was recorded using a 128-electrode Hydrocel Geodesic Sensor Net System (EGI Inc) and adequate data was gathered on 14 children in each group. Analysis was focused on the differential neural response to the social and non-social conditions, with variables of interest including the frontal N1, Pb and Nc.

Results: TD children were overall more social than the ASD group. The ASD group, however, did show evidence of having detected the difference in the examiner's behavior between the two conditions, as they were significantly less engaged in the non-social condition when the examiner withdrew interaction with the child. In the EEG analysis, TD children demonstrated differentiation of conditions based on their left Nc amplitude, with a larger (more negative) response to the non-social condition, suggesting that greater attention resources were required to process objects lacking social salience. In contrast, children with ASD did not differentiate the conditions. Finally, in the TD group, attempts to initiate eye contact correlated with N1 amplitude difference by condition, suggesting that interaction with a responsive social partner facilitates learning in typical development.

Conclusions: These results suggest that social cues do not seem to facilitate object processing in young children with ASD, and they illustrate a disconnect between overt behavior and information processing in this population. This type of investigation will be critical to determine if learning deficits not only predict response to specific interventions but also whether they can be modified through treatments targeting joint attention and social engagement.

**117.003 3** A Novel fMRI Paradigm for Testing Learning in Adolescents with ASD. M. Solomon[1], J. C. Matter*[2], T. A. Niendam[3], T. A. Lesh[4], J. S. Beck[5], C. S. Carter[3] and J. D. Ragland[4], (1)*Department of Psychiatry, MIND Institute, Imaging Research Center*, (2)*UC Davis MIND Institute*, (3)*UC Davis, Psychiatry*, (4)*Imaging Research Center*, (5)*UC Davis*

Background:

Deficits in learning are central to Autism Spectrum Disorders (ASD). One type of learning deficit found in affected individuals is the inability to *generalize* (or transfer) what they have learned during training to new similar situations. Generalization problems have a profound impact on the academic, social, and adaptive functioning of persons with ASD, and have not been well studied.

Objectives:

We sought to advance our understanding of the cognitive and neural basis of generalization deficits in adolescents with ASD using a transitive inference (TI) paradigm which has been well characterized in typically developing individuals. TI involves learning a series of ordered stimulus pairs (AB, BC, CD, DE, EF where A>B>C>D>E>F), and then transferring or generalizing this learning about order to novel pairs (AC, AD, AE, BD, BE, CE).

Methods:

Participants were 25 medication free adolescents with ASD aged 12-18 evaluated using gold standard ASD diagnostic measures, and 25 age, gender, and IQ matched adolescents with typical development (TYP). We implemented a rapid event-related functional magnetic resonance imaging (fMRI) study of a new TI paradigm for adolescents, with a 5-stimulus pair hierarchy, a game format, frequent feedback, and prizes. Whole brain voxel-wise analyses were conducted using SPM8. We also interrogated regions of interest in the striatum, prefrontal cortex (PFC), and medial temporal lobes, and conducted functional connectivity analyses using these regions as seeds. Based on our prior study of TI (Solomon, Frank, Smith, Ly, & Carter, 2011), we hypothesized that: (1) ASD group performance would be associated with the use of a rote memory strategy involving the hippocampus and visual cortical brain regions; (2) TYP group performance would be associated with recruitment and functional connectivity of the striatum, prefrontal cortex (PFC), and the parietal cortex; and that (3) task performance would be related to math and reading achievement test scores.

Results:

Both groups learned the task to comparable rates by the end of training. At test, the ASD group outperformed the TYP group on the most difficult previously trained CD pair, suggesting they showed superior rote memory. Whole brain and ROI analyses revealed the ASD group exhibited greater medial temporal lobe activation during training that was related to later inference pair performance. At test, there was less activation in prefrontal regions in the ASD group on inference versus premise pairs. However, there was greater evidence of functional connectivity with visually related brain regions in the ASD versus the TYP group that was associated with task performance suggesting these brain regions were used in a compensatory fashion. Indices of cognitive control deficits were related to deficits in reading comprehension and math problem solving.

Conclusions:

ASD rely on a rote learning-based strategy as opposed to a more flexible one that can incorporate rapid updating of reward contingencies, and integrate this information in the service of generalization. This interpretation is supported by the systems-level computational modeling work of Frank et al. (2004, 2005, 2006), and also is consistent with the underconnectivity theory of ASD proposed by Just, Cherkassy, Keller & Minshew, 2004.

**117.004 4** Visual-Motor Functional Connectivity Relates to Autism Severity. M. B. Nebel*[1], A. Eloyan[2], C. Nettles[1], K. Ament[1], K. L. Sweeney[1], R. Ward[1], A. S. Choe[1], A. D. Barber[3], B. S. Caffo[2], J. J. Pekar[1] and S. H. Mostofsky[3], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Johns Hopkins School of Medicine*

Background: Autism Spectrum Disorder (ASD) affects many areas of skill development, including motor skills. Research suggests that motor, communication, and social skill learning may share a common brain-basis. ASD-associated deficits in imitating others' actions, dependent on visual-motor integration, likely impact both motor and social skill acquisition; however, it is unclear what brain mechanisms contribute to these deficits.

Objectives: To investigate the relationship between visual-motor functional connectivity (FC) and both imitation ability and autistic trait severity in children with ASD.

Methods: Resting state (rs) fMRI scans were collected from 100 children (50 ASD; 50 typically developing [TD]). Data were interpolated to account for slice acquisition order, and rigid body realignment parameters were estimated with respect to the first functional volume to adjust for motion. Anatomical images were registered to the first functional volume and then to the MNI template. The estimated rigid body and non-linear spatial realignment transformations were then applied to the rs data. Linear trends were removed from the rs data and a Gaussian filter (6-mm FWHM kernel) was applied. Voxel timeseries were intensity-normalized to have a mean of 100. All 100 rs scans were combined to estimate visual and motor networks using independent component analysis. Participant-specific spatial maps and timeseries were back-reconstructed from the group-level components. To estimate visual-motor FC, Pearson correlations between each pair of participant-specific motor and visual network timeseries were computed and converted to z-scores using Fisher's transform. Brain-behavior relationships were assessed by regressing visual-motor FC with imitation and autistic trait severity scores. Imitation ability was assessed using the Florida Apraxia Battery; scores reflected the number of imitative gestures performed correctly. Autistic trait severity was assessed using the Social Responsiveness Scale (SRS); higher scores indicated more severe autistic traits.

Results: Two motor networks (dorsal [DM] and ventral [VM]) and three visual networks were identified. Two visual networks included early visual processing areas (BA 17 and 18), while the third (VC3) included higher-order visual areas involved in perspective processing. In children with ASD, VM was more negatively correlated with VC3 (-.12) compared to TDs (.08, $p < .05$ corrected), and the strength of this coupling was inversely correlated with total SRS score in the ASD group ($R=-.42$, $p=.004$). In TDs, stronger VM-VC3 FC was associated with better imitation ($R=.41$, $p=.01$) and better overall performance of gestures on praxis examination ($R=.61$, $p<.001$). No relationship was observed between visual-motor FC and imitation ability in ASDs.

Conclusions: Children with ASD exhibited significantly stronger negative functional coupling between motor and higher-order visual areas compared to their TD peers, and the strength of this negative coupling was associated with the severity of autistic traits. Children with stronger negative coupling between motor and higher-order visual areas demonstrated more severe autistic traits. In TD children, motor-visual FC strength was correlated with imitation performance; children with stronger positive visual-motor coupling were better imitators. The findings suggest that visual-motor connectivity is associated with the ability to imitate others actions, and that for children with ASD, decreased visual-motor connectivity may contribute to impaired social skill development

**117.005 5** Changes in Brain Activation and Connectivity in Children with Autism before and after a Visualization Language Intervention. D. Murdaugh*, A. R. Lemelman, H. D. Deshpande, S. E. O'Kelley and R. K. Kana, *University of Alabama at Birmingham*

Background: Deficits in language comprehension have been widely reported in children with autism spectrum disorders (ASD). Recent evidence from neuroimaging research suggests that people with ASD tend to recruit visuospatial imagery to comprehend language (Kana et al., 2006). Such increased reliance on visuospatial regions may also underlie weaker coordination between primary visual and association areas.

Objectives: This fMRI study investigates the brain activation and connectivity patterns in ASD during language comprehension. The main objective was to determine the impact of a 10-week visualizing language intervention on improving functional activation and connectivity during a visual imagery language task in children with ASD.

Methods: 32 children with ASD (ages 8-13 years) were imaged twice 10 weeks apart, with 17 children receiving the intervention soon after the initial fMRI scan, and 15 wait-list control children. In addition, 27 typically-developing (TD) children, age and IQ-matched, were imaged once. A language comprehension task, presented while the children underwent fMRI, included high and low imagery sentences. The data were used to investigate intervention related effects on brain activation and connectivity. Data were acquired from a Siemens 3.0T Allegra head-only scanner and analyzed using SPM8.

Results: (1) Between-group analysis of the ASD groups at their pre-imaging session and typically-developing (TD) controls revealed differences in high-imagery sentences, with the ASD group recruiting Wernicke's area (BA 40) and right precentral and right lingual gyri; (2) Specific differences were found in the visual word form area of the mid-fusiform region, with the ASD group failing to activate this area pre-imaging session; (3) Children with ASD who received the intervention between imaging sessions showed increased activation in the right middle occipital gyrus and lingual gyrus pre- to post-imaging session. There were no significant pre- to post-imaging session differences in the wait-list control group; (4) Between-group results revealed greater activation in the intervention group as compared to the wait-list control group in both language regions and frontal regions ($p<0.001$, cluster corrected); (5) A functional connectivity analysis revealed greater synchronization between the medial prefrontal gyrus and a number of language and visual association brain regions in the children with ASD who received the intervention compared to the wait-list controls.

Conclusions: This study introduces a novel and intensive language-based remediation treatment that is designed to use nonverbal sensory input, an area relatively intact in individuals with ASD, in order to develop oral and written language comprehension, establish vocabulary, and develop higher order thinking skills. The results of this study reveal that children with an ASD who received the V/V intervention show increased activity in visual language association regions post-intervention. In addition, when compared to our wait-list control group, the children with ASD who received the intervention showed greater activity in language and frontal regions and greater connectivity between frontal and more posterior language and visual areas. Our preliminary findings reveal the plasticity of the brain in children with autism, and suggest improvement of neural activity and synchronization due to targeted intervention.

**117.006 6** Novel Network Estimation Tools Extract Common ASD Features from Abide Dataset. S. N. Tomson*[1], M. Narayan[2], G. I. Allen[3], S. Y. Bookheimer[1] and M. Dapretto[1], (1)*UCLA*, (2)*Rice University*, (3)*Jan and Dan Duncan Neurological Research Institute*

Background: Functional connectivity studies have recently gained momentum in autism

spectrum disorder (ASD) research, but the phenotypic diversity and inherent inter-subject variability in ASD populations have produced widely varying results in network metrics. This incongruity might be solved by exploring two primary methodological challenges: what is the most reliable way to measure functional connections, and how do we quantify differences between group-level networks with hundreds of nodes and thousands of edges? We seek answers to these methodological questions in ASD and neurotypical populations, with the goal of working toward a diagnostic biomarker.

Objectives: The goal of this work is to develop new statistical models to address the heterogeneity in high dimensional ASD neuroimaging data sets. We propose novel methods of quantifying resting state networks in functional MRI data, and we compare our results to existing findings in the ASD literature.

Methods: To address this challenge, we studied resting state fMRI data from the Autism Brain Imaging Data Exchange (ABIDE). All individuals with ASD (N=35, Controls N=43) had an ASD diagnosis confirmed using the Autism Diagnostic Observation Schedule (ADOS). We employed Gaussian Markov Networks to estimate direct connections between nodes using partial correlation (Smith et al. 2002). Partial correlations offer estimates of "direct" functional connections, eliminating correlations from indirect influences. To determine the sparsity of the network, we adapted a statistical technique called stability selection, which enforces the sparsity level that retains the most stable edges (Liu et al. 2010). We used block-bootstrapping and resampling to compare the networks, then performed a resampling and randomized regularization procedure to determine how often individual edges were present in each group. We used Storey's method (Storey 2002) to estimate the false discovery rate, and we report here 7 of the most strongly differential edges of the 235 edge level hypotheses tested.

Results: Our results support three common trends in the ASD literature: decreased inter-hemispheric communication, reduced long-range connectivity, and fewer connections with the inferior frontal and fusiform gyri in ASD. These findings were derived using statistical techniques specifically designed for high dimensional data to 1) account for inter-subject variability and 2) appropriately address multiple testing corrections. Our methods are now freely available online as the Markov Network Toolbox (MoNeT) for functional connectivity estimation.

Conclusions: We suggest novel methods for estimation of functional connectivity networks, and we provide evidence that these methods produce results in line with prior findings in the ASD literature. Future goals include analyzing several ABIDE datasets and comparing across samples to identify common network features in ASD.

**117.007 7** Brain Activity and Local Connectivity Underlying Action Understanding in Autism Spectrum Disorders. J. O. Maximo*[1], L. E. Libero[1] and R. K. Kana[2], (1)*University of Alabama Birmingham*, (2)*University of Alabama at Birmingham*

**Background:** Detecting the means (*how*) and intent (*why*) of others' actions may involve motor simulation of their action, possibly mediated by the mirror neuron system. Another neural network that may be involved in this process is the theory-of-mind (ToM) network consisting of regions, such as the temporoparietal junction (TPJ), superior temporal sulcus (STS), and medial prefrontal cortex (MPFC). While functional deficits in both of these systems have been reported in people with ASD, they are seldom studied in conjunction.

**Objectives:** The main objective of this study was to characterize the neural network involved in interpreting the *how* and *why* of actions in high-functioning adults with ASD

**Methods:** fMRI data were acquired from 24 high-functioning adults with ASD and 26 typically developing (TD) control participants while they made action and intention judgments about a series of static images of a model using household objects. The participants' task was to view the model's action and determine whether the means (how the action was carried out) or intent (the model's goal) of the action was ordinary or unusual. fMRI data were preprocessed using AFNI and FSL. Local connectivity was calculated using the Regional Homogeneity (ReHo) approach for every voxel and its 26 immediate neighbors. This analysis included low-pass filtering, "scrubbing", and removal of task-related effects. In addition, parameter estimates extracted from activated brain regions were correlated with assessment

scores (Reading the Mind in the Eyes [RME] test, Empathy Quotient [EQ], and the Ritvo Autism Asperger Diagnostic Scale-Revised [RAADS-R]) to establish brain-behavior relationships.

**Results:** Overall, interpreting unusual actions generated more activity in both ASD and TD groups, compared to ordinary actions. The TD participants, relative to ASD adults, showed increased activation in right middle frontal gyrus while processing unusual actions. The ASD group, on the other hand, showed increased activation in left middle occipital area for processing intentions. ReHo analysis revealed overconnectivity in participants with ASD in right middle frontal gyrus ($p$ <.05, FWE corrected). Significant positive correlations were found between the RME scores and activation in left fusiform and bilateral superior temporal gyri (STG) in the TD groups; ASD group showed positive correlation between RME and right fusiform activation.

**Conclusions:** Our findings of altered activation in occipital and frontal regions in the ASD group may suggest more strategic and visual approach to interpret actions. The overconnectivity in RMFG (BA8, BA9) in participants with autism is consistent with previous findings of excess frontal connectivity (Courchesne & Pierce, 2005), increased neuron number (Courchesne et al., 2011), and increased number of cortical minicolumns (Casanova, 2004) in frontal regions in ASD. While TD participants had a significant positive predictive relationship between RME scores and STG activity, this relationship was not seen in ASD adults, perhaps suggesting their reliance on altered neural routes in reading intention from action. Given that we did not find a group difference in mirror neuron system activity, this neural system may not differ in high-functioning ASD individuals while interpreting others' actions.

**117.008 8** Regionally Specific Resting-State Alpha Oscillatory Abnormalities Predict Clinical Impairment in Autism Spectrum Disorders. J. C. Edgar*[1], Y. Chen[1], J. Herrington[2], V. Y. Chow[1], L. Bloy[1], J. Pandey[3], R. T. Schultz[3] and T. P. Roberts[1], (1)*Children's Hospital of Philadelphia*, (2)*The University of Pennsylvania*, (3)*The Children's Hospital of Philadelphia*

**Background:** A disruption in the excitatory/inhibitory balance of neural activity is increasingly thought to characterize autism spectrum disorders (ASD). Despite cellular and molecular evidence (Rubenstein and Merzenich 2003), very few studies to date have investigated an excitatory/inhibitory imbalance in ASD at a macroscopic cortical circuit scale. This putative imbalance can be assessed noninvasively during a resting-state (RS) exam via patterns of neural oscillations, as oscillatory activity reflects the synchronous firing of large populations of neurons mediated by excitatory/inhibitory interactions. In a previous study, our laboratory observed increased parietal-occipital RS alpha activity in non-medicated children with ASD, with increased alpha power associated with higher scores on the Social Responsiveness Scale (Cornew et al. 2012).

**Objectives:** The present studies sought to replicate and extend our previous findings, examining a new and larger sample of ASD and typically developing children (TDC). In addition, rather than obtaining lobar measures of alpha activity, estimates of RS alpha activity were obtained throughout the brain.

**Methods:** RS whole-head magnetoencephalography (MEG) was obtained from forty-seven male TDC and forty-one male ASD participants. RS activity was analyzed using a lead-field-based source localization method, Vector-based Spatio-temporal Analysis using L1-minimum norm (VESTAL). Group differences in alpha power and alpha peak frequency were examined. Given a well-documented association between alpha peak frequency and age, hierarchical regressions examined associations between alpha peak frequency and age.

**Results**: The ASD group had more alpha activity than the TDC group in regions bordering the Central Sulcus as well as parietal association cortices ($p < 0.05$). In ASD, stronger left Central Sulcus alpha power was associated with higher Social Responsiveness Scale scores ($p < 0.05$). In both groups the strongest alpha activity was observed in regions bordering both sides of the Calcarine Sulcus. In the Calcarine Sulcus, only the TDC group showed the expected association between age and alpha peak frequency ($p < 0.05$).

**Conclusions**: The observation of increased RS alpha activity in primary motor and somatosensory areas in the present study suggests that the ASD brain is potentially underprepared for sensory input. Given the modulating influence of the thalamus on RS alpha

activity, findings suggest the possibility that thalamic abnormalities are primary to RS alpha abnormalities in ASD. MEG + DTI studies examining associations between the Central Sulcus and Calcarine Sulcus alpha rhythms and lateral geniculate nucleus and ventral posterior nucleus thalamocortical pathways are of interest.

**117.009 9** Intra-Individual Variability in Behavioural and fMRI Sensory-Evoked Responses in Autism. S. M. Haigh*[1], D. J. Heeger[2], I. Dinstein[3], N. J. Minshew[4] and M. Behrmann[1], (1)*Carnegie Mellon University*, (2)*New York University*, (3)*Ben-Gurion University*, (4)*University of Pittsburgh School of Medicine*

Background: Autism is a neurodevelopmental disorder that affects neural circuitry across the brain. One indicator of altered cortical processing in autism is greater variability in sensory-evoked responses (found using fMRI and EEG) from one trial to the next, suggesting unreliable sensory-evoked responses (Milne, 2011; Dinstein et al., 2012).

Objectives: To confirm the greater variability in fMRI sensory-evoked responses across sensory modalities in autism and to investigate the functional significance of the greater cortical variability in ASD by assessing variability in roughness perception. A subgroup of participants with ASD participated in both experiments to allow for direct comparison between cortical and behavioural responses.

Methods: Two experiments were conducted. For experiment 1, we used the same method as reported by Dinstein et al. (2012), to measure the visual (moving white dots), auditory (pure tone beeps) and somatosensory responses (air puffs to the back of the hand) in primary sensory cortices in a new group of individuals with autism. Each stimulus was repeated 24 times over two scanning sessions. The data from the original study by Dinstein et al. (2012) were used to compare the responses from the new autism group (N=12) to the original autism group (N=14). For experiment 2, 17 individuals with autism and 17 age- and gender-matched control were asked to rate 12 surfaces on roughness using a Likert scale of 1 (not very rough) to 10 (very rough). Each plate was presented 14 times to gauge a measure of variability. A sub-set of individuals with autism took part in both experiments (N=13).

Results: For the roughness experiment, we found that the individuals with autism perceived the surfaces as rougher and were more variable in their ratings (from trial to trial) compared to matched controls. For the fMRI study, we found similar results in the new autism group compared to the original autism group (from Dinstein et al., 2012): greater trial-to-trial variability in sensory-evoked responses and weaker SNR compared to typical individuals. For the sub-group of individuals with autism who took part in both roughness perception and fMRI experiments, those with greater fMRI response variability rated the plates as feeling rougher, suggesting a functional correlate of the variable sensory responses, and their contribution to the sensory sensitivities that are commonly associated with autism. In addition, greater variability in the roughness ratings was associated with greater fMRI response variability in the visual cortex. This was despite participants wearing headphones playing white noise and an eye mask. This is consistent with the hypothesis that visual imagery is used to help interpret tactile stimuli, and consequently, that greater response variability in visual cortex may impact tactile perception.

Conclusions: Individuals with autism produce more cortical and behavioural intra-individual variability than controls, and variability in fMRI responses correlates with behavioural responses. This suggests that there is a functional consequence of the greater intra-individual variability, and that the variability is an endophenotype in autism. Unreliable sensory responses could contribute to the unusual sensory sensitivities that are a part of the DSM-V criteria for autism.

**117.010 10** Hyperconnectivity of the Right Posterior Temporo-Parietal Junction Predicts Social Deficits in High-Functioning Boys with Autism. H. Y. Lin*[1], H. Y. Chien[2], M. C. Lai[3], W. Y. I. Tseng[2] and S. S. F. Gau[2], (1)*National Taiwan University Hospital*, (2)*National Taiwan University College of Medicine*, (3)*University of Cambridge*

Background: Autism is characterized by impaired social cognition, which may be underpinned by systems-level atypical neural connectivity. The posterior right temporo-parietal junction (pRTPJ) is a key region involving in representing other's mental states. In neurotypical individuals, the pRTPJ exhibits intrinsic functional connectivity (iFC) with areas associated with social cognition (e.g., the default mode network, DMN). Atypical

activation at pRTPJ during mentalizing in individuals with autism has been shown, however the iFC of the pRTPJ remains underexplored.

Objectives: We test whether boys with autism show altered resting-state iFC of the pRTPJ. We further test whether atypical iFC of pRTPJ is associated with social deficits in autism.

Methods: Resting-state fMRI (3-Tesla Siemens Tim Trio system, 6-minute scan with eyes closed, TR=2sec) was collected in 46 boys with autism and 44 typically developing (TD) boys. Participants exhibiting greater than 4 time points of excessive in-scanner head motion of frame-wise displacement >1mm were excluded from analyses. The final sample included 40 boys with autism (aged 9-17 years, mean age=12.38±2.17; mean PIQ=105.60±16.06), and 42 age- and performance IQ-matched TD boys (mean age=11.64±2.71; mean PIQ=111.29±13.45). Data were preprocessed using the Data Processing Assistant for Resting-State fMRI (DPARSF) toolbox based on SPM8, without regressing out mean global signals. Motion artifact was corrected by nuisance regression against 24-autoregressive motion parameters at an individual level, together with individual mean frame-wise displacement included as a covariate in the group-level analysis. Seed-based approach was used to investigate iFC (i.e., Pearson's correlation between time-series) of the pRTPJ. General linear model was used to analyze between-group differences in iFC, cluster-wise FWE-corrected at $p<0.05$, with a cluster-forming voxel-level threshold of $p<0.01$. Pearson's correlations between atypical iFC (seed-peak atypical coordinate pairs) in the autism group and social difficulties measured by the Chinese version of the ADI-R and Social Responsiveness Scale (SRS) were calculated, corrected for multiple comparisons at FDR $q<0.05$ (an FDR q between 0.05-0.1 was considered trend-level significant).

Results: TD boys demonstrated a resting-state pRTPJ iFC pattern comparable to the known spatial involvement of the DMN, which was not reliably observed in boys with autism. Boys with autism showed pRTPJ *hyperconnectivity* relative to TD boys in a right-hemispheric cluster (9693 $mm^3$) involving the lingual gyrus (LG), fusiform gyrus (FG), and middle occipital gyrus (MOG), each with a group-difference peak. There was no increased connectivity of the pRTPJ in TD boys compared to boys with autism. There were significant positive correlations between the pRTPJ-right MOG connectivity and total SRS score ($r=0.36$, $q=0.048$), and the 'social communication' ($r=0.38$, $q=0.045$) and 'social emotion' ($r=0.38$, $q=0.045$) subscores of the Chinese SRS. pRTPJ connectivity with other two subregions showed trends of positive correlations with the same Chinese SRS scores ($r=0.23$-$0.29$, $q=0.083$-$0.091$). There was a positive correlation between social reciprocity deficits on the ADI-R and pRTPJ-right FG connectivity ($r=0.34$, $q=0.051$).

Conclusions: We found resting-state hyperconnectivity between pRTPJ and right occipito-temporal regions in high-functioning boys with autism, which was correlated with their social deficits. This indicates that atypical connectivity of the pRTPJ may be integral to the atypical neurobiology of autism.

**117.011 11** Sex-Modulated Atypical Resting-State Functional Connectivity in Autism: An Independent Component Analysis.

R. A. Bethlehem*[1], M. C. Lai[1], M. V. Lombardo[2], A. N. Ruigrok[1], B. Auyeung[1], J. Suckling[1], E. Bullmore[1], M. AIMS Consortium[3], S. Baron-Cohen[1] and B. Chakrabarti[4], (1)*University of Cambridge*, (2)*University of Cyprus*, (3)*Institute of Psychiatry, King's College London; Autism Research Centre, University of Cambridge; Autism Research Group, University of Oxford*, (4)*University of Reading*

Background: Atypical neural connectivity has been proposed to be a potential hallmark for autism, with hypotheses including decreased fronto-posterior and enhanced parietal-occipital connectivity, reduced long-range and increased short-range connectivity, and temporal binding deficits. However, empirical findings vary substantially depending on the aspects of connectivity examined, the developmental stage of the individual, the spatial and temporal scales, task versus no-task conditions, how motion artefacts are handled, and the specific neural systems of concern. In addition, the role of biological sex in modulating atypical connectivity in autism is not yet clear.

Objectives: (1) To explore the atypical connectivity hypothesis of autism using functional connectivity (FC) analysis on resting-state functional magnetic resonance imaging (fMRI) data, using a non-biased, model-free, data-driven approach: independent component analysis (ICA);

(2) To explore if biological sex modulates the characteristics of resting-state FC in autism.

Methods: Resting-state fMRI data (3T, 13 minutes with TR=1302 ms, eyes closed) from 117 individuals in four groups (males with autism N=25, neurotypical males N=33, females with autism N=30, neurotypical females N=29), matched for age, IQ and in-scanner head-motion, was analyzed with ICA using the Group ICA Toolbox (running under Matlab). We investigated 29 components, out of a total of 59 estimated independent components, that showed a high goodness-of-fit with known resting-state networks (for the remaining components, 17 were labelled undetermined and 13 likely reflected aliasing noise signal or artefact). To test group differences in within-component FC, two-way factorial ANCOVAs (factor 1: diagnosis [autism, neurotypical], factor 2: sex [male, female]) were performed for the 29 component maps of interest, with age and average frame-wise displacement as nuisance covariates. Using permutation tests, we further compared group differences in FC between all 46 non-artefactual components.

Results: For within-component FC, main effects of diagnosis and sex were found in both directions, on almost all components that were examined. In brief, we found functional decoupling between the precuneus and the anterior cingulate in the autism group, as well as decreased coupling between the basal ganglia and medial prefrontal cortex. However, diagnosis-by-sex interactions were almost ubiquitously seen in regions other than those showing main effects. For between-component FC, the default mode network components were more functionally connected to other components in the male autism group compared to the male neurotypical group. This difference, however, was not apparent in the female group.

Conclusions: Results revealed evidence for atypical but heterogeneous connectivity in high-functioning adults with autism compared to neurotypical adults. The directionality of differences in within-component FC varied substantially with components. In addition, biological sex significantly modulated the effect of diagnosis in most components. Overconnectivity between the default mode network components and other components was found in autism, but only in males. Overall these indicate a complicated picture of atypical connectivity in autism, which at the same time substantially differed between males and females. More fine-grained descriptions on patterns of atypical connectivity in different subgroups of autism are needed, as opposed to an over-simplified view that general hypo- or hyper-connectivity marks the atypical neurobiology of autism.

**117.012 12** Are the Neural Attunement Effects of Oxytocin Related to Naturalistic Changes in Communicative Behavior Following Administration to Children with ASD?. I. Gordon*[1], B. C. Vander Wyk[1], R. H. Bennett[2], C. Cordeaux[1], M. V. Lucas[1], J. F. Leckman[1], R. Feldman[3] and K. A. Pelphrey[1], (1)*Yale University*, (2)*Yale Child Study Center*, (3)*Bar-Ilan University*

Background: Discoveries regarding the behavioral impact of acutely modulating the neuropeptide oxytocin (OT) have led to exciting avenues for translational research efforts in autism spectrum disorders (ASD). Novel reports on the neural mechanism involved in intranasal administration of OT to individuals with ASD highlight OT's positive impact on key nodes of "the social brain" such as the amygdala and the medial prefrontal cortex. Despite the highly significant effects OT seems to have on brain function, behavioral results at times have been modest, especially when measured within the context of brain imaging paradigms or when OT is given chronically. Considering the positive impact acute manipulation of OT has had on various social behaviors, such as emotion recognition and theory of mind, it is crucial to achieve a crystalized understanding of the associations between the neural impact of intranasal OT and the resulting changes in naturalistic social-communicative behaviors in ASD.

Objectives: In an fMRI study, we aimed to pinpoint the neural mechanism underlying a single OT administration in children with ASD. We further aim to identify and describe the associated impact of OT on communicative behaviors in naturalistic social interaction settings. We expect neural effects of OT administration to be positively related to improvements in patterns of social behavior, such as eye gaze pattern and positive affect, during interactions with participants' parents. We hypothesize that interactions between children and parents will become more synchronized with the social partners in line with the neural impact on brain function after OT administration.

Methods: Seventeen children with ASD (ages 7-18) received acute administration of OT in this placebo-controlled study of changes in brain activity and behavior. Following OT, a behavioral interaction between youth and their parents was recorded and an fMRI scan ensued in which a well-validated fMRI paradigm for social processing was presented. fMRI data was analyzed to assess the neural impact of OT. We are currently micro-analyzing videotaped behavioral interactions between youth and their parents for aspects of social functioning, such as gaze patterns, arousal, proximity, touch, repetitive behaviors and self-regulatory functions.

Results: Results from brain function analysis indicate that OT increased activity in the striatum, the middle frontal gyrus, the medial prefrontal cortex, the right orbitofrontal cortex, and the left superior temporal sulcus. In the striatum, nucleus accumbens, the left posterior superior temporal sulcus, and the left premotor cortex, oxytocin increased activity during social judgments and decreased activity during non-social judgments. All of these regions have previously been implicated in their involvement in social perception and cognition, mentalizing abilities, and theory of mind. We will also present first-ever reported behavioral outcomes micro-analyzed from videotaped parent-child interactions and their association with brain imaging results.

Conclusions: These results will provide essential and critical steps in the integrative understanding of the neural and behavioral impact a single administration of intranasal OT has in youth with ASD. This will advance novel and more effective treatments for core social deficits in ASD.

**117.013 13** Neural Habituation in Response to Emotional Faces and Houses in ASD. N. M. M. Kleinhans*[1], T. L. Richards[1], J. Greenson[1], G. Dawson[2] and E. H. Aylward[3], (1)*University of Washington*, (2)*Duke University*, (3)*Seattle Children's Research Institute*

Background: Previous work has shown that abnormal amygdala habituation to faces is a robust indicator of ASD dysfunction and associated with individual differences in social impairments. However, the generalizability of the habituation effect to other classes of stimuli is unknown.

Objectives: To determine whether atypical neural habituation in ASD is a face-specific or a domain-general mechanism present across visually complex objects such as houses.

Methods: We performed a secondary analysis of previously published and unpublished fMRI data designed to follow-up and extend our previous work on habituation in ASD. Twenty-seven adults with an ASD and 25 age and IQ matched controls were included. Two identical block-design fMRI runs were collected (Time 1=T1, Time 2=T2). Masked fearful faces ("F"), masked houses ("H"), and scrambled images ("S") were presented. Six, first-level analyses were conducted $F_{T1}>S_{T1}$; $F_{T2}>S_{T2}$; $H_{T1}>S_{T1}$; $H_{T2}>S_{T2;}$ $F_{T1}>H_{T1;}$ and $H_{T1}>F_{T1}$. Functional localizers for the Face (lateral fusiform) and House (medial fusiform) areas were created based on the entire study sample (N=54) for the contrasts $F_{T1}>H_{T1}$ and $H_{T1}>F_{T1}$. Anatomically-based right and left amygdala masks were also utilized. The average z-score within each mask was computed for each contrast. In addition, habituation was computed for each mask by subtracting T1-T2. Average z-scores and habituation scores were imported into Predictive Analytics SoftWare Statistics 18.0.0.

Results: We investigated the role of stimulus-type, brain region, and diagnosis on habituation rates. A 2x2x4 repeated measures ANOVA was conducted with diagnosis as the between-group variable and time ($T_1$ vs. $T_2$) and brain region (right/left amygdala, right lateral fusiform, right medial fusiform) as the within-subject variables. The dependent variable was average z-score, which was nested under the 16 variables. The three-way interaction was significant ($F=3.808$, $p=.016$). In addition, we found a diagnosis by time interaction ($F=18.53$, $p=.000$) and a brain region by time interaction ($F = 3.027$, $p = .038$) but no significant interaction between brain region and diagnosis ($F=.399$, $p=.755$). Follow-up tests reveal that the ASD group showed significantly less habituation to faces in the right amygdala ($F=8.317$, $p=.006$), left amygdala ($F=30.521$, $p<.000$) right lateral fusiform ($F=4.612$, $p =.037$). There was no group-by-time interaction effect for houses in the right medial fusiform ($F=.733$, $p=.396$). We evaluated the diagnostic discriminability of our habituation score for each brain region using Receiver Operating Characteristic curves. Left amygdala habituation to fearful faces had the strongest predictive value (AUC = .852, p<.000); a threshold of habituation score ≤ 0 (indicating no change in activation

across time) detected 21/27 (78%) participants with ASD and correctly excluded 16/25 (64%) of controls. Habituation to houses had no predictive value (AUC = .573, p =.365).

Conclusions: These results suggest that reduced habituation in ASD is specific to emotional stimuli and especially pronounced in the amygdala. Fearful face activation in the amygdala shows a unique group-by-time interaction effect, characterized by a pattern of decreased activation in the TD group, and increased activation in the ASD group. We propose that amygdala habituation to emotional faces may be an effective biomarker for quantifying risk at the individual level in ASD.

**117.014 14** Phase Reset As a Biomarker of ASD. J. Frohlich*[1], K. McEvoy[2] and S. S. Jeste[2], (1)*University of California, Los Angeles*, (2)*UCLA*

Background: Rigid, inflexible behavior and interests represent a core deficit in autism spectrum disorder (ASD). Whether inflexible behavior is reflective or resultant of inflexible brain dynamics, as measured by electroencephalography (EEG), remains an open question in autism research. Prior work by Thatcher and colleagues (2009) has shown that children with ASD, aged 2.6 – 11 years, generally have longer durations of phase locking between EEG channels than those with typical development. We hypothesize that EEG dynamics in individuals with ASD exhibit greater metastability than those of typically developed (TD) individuals as measured by number of state transitions. Analytic phase serves as a useful state variable for detecting state transitions (specifically, "phase resets").

Objectives: Our principal objective is to characterize the phase reset of resting state EEG in young children with ASD and to explore the heterogeneity in phase reset, with particular interest in the association between phase reset and severity of repetitive behaviors and inflexibility in this population. Specifically, we wish to correlate the number of phase resets (an inverse measure of metastability) in resting state EEG with repetitive behavioral symptoms. We also wish to correlate number phase resets with age. Doing so will not only allow effects of age to be regressed out, but will also allow changes in metastability to be cross-sectionally mapped through typical development.

Methods: Children with ASD and TD controls, ages 2-6, were recruited through the UCLA Center for Autism Research and Treatment (CART). Resting state EEG data were cleaned for artifacts and analyzed using the Hilbert transform, a linear transform for computing the analytic phase and analytic amplitude of a time series. By dividing the unwrapped analytic phase by 2π and computing the second derivative with respect to time, i.e., the rate of linear frequency change, one can inspect the new signal for large "spikes" indicative of phase resets. Such phase resets are spatiotemporally correlated. Counting spatiotemporal clusters of phase resets in low gamma (30-50 Hz) band resting state EEG datasets quantifies their metastability as a consequence of the inverse relationship between metastability and number of phase resets.

Results: After disqualifying datasets with excessive EMG artifacts and bootstrapping pilot data from 12 ASD (aged 27-72 months, mean = 49 months) and 9 TD subjects (aged 31-74 months, mean = 56 months), we found a trend of greater metastability in ASD subjects (not significant, $p = 0.083$). No significant difference was found between ages of TD and ASD subjects using Student's $t$-test ($p = 0.3$). Examining only subjects at least as young as the median age (53 months) and bootstrapping gave a similar but nearly significant result ($p= 0.051$).

Conclusions: Metastability as measured by spatiotemporal clusters of phase resets in frequency filtered resting state EEG shows potential as a biomarker of ASD. Future work will focus on discriminating between different subpopulations in ASD, as well as cross-sectionally mapping changes in metastability in the TD population.

**117.015 15** Concordance in Inhibitory Event Related Potentials Among Twins with and without Autism. S. Faja*, A. Kresse, E. E. Neuhaus, C. Sonners, R. Bernier and S. J. Webb, *University of Washington*

Background: Concordance rates among twins provide evidence that genetic factors contribute to risk for autism spectrum disorder (ASD). Twin studies may also be informative about potential endophenotyes in ASD. One potential endophenotype, response inhibition, is a core executive function. Inhibition is related to cognitive flexibility, which is impaired in autism (Russo et al 2007). Anokhin et al (2004) identified

heritability estimates for the inhibitory paradigm (Go/No-Go) event-related potential (ERP) responses N2 and P3 at 60% and 41%, respectively, in an adult non-affected twin sample. However, heritability in twins with ASD has not been examined. The current study uses neurophysiological measurement (ERP) to explore the correlation between N2 and P3 responses in twins with ASD and typical development (TD). The N2 and P3 are related to monitoring and inhibition, respectively.

Objectives: This study examined correspondence within monozygotic (MZ) twin pairs relative to dizygotic (DZ) twin pairs during a Go/No-Go task for the N2 and P3 ERP components. Stronger correspondence within MZ twin pairs relative to DZ pairs would provide support for genetic contributions to this domain.

Methods: The sample included 12 MZ and 6 DZ twin pairs with typical development and 8 MZ and 6 DZ twin pairs with ASD. Twins ranged in age from 7 years to 22 years (mean = 12.1 years). Electrophysiological responses were continuously recorded with high-density EEG as twins completed a Go/No-Go task with shapes. The average mean amplitude for the N2 at Fz and P3 at Pz was obtained for each twin in the Go and No-Go conditions.

Results: Among MZ twins with TD, a significant relation was detected in the N2 Go condition, $r(12) = .69$, $p = .01$ and no relations were detected among DZ twins with TD. Among MZ twins with ASD, a trend was detected in the N2 Go condition, $r(11) = .87$, $p = .06$. In addition, the DZ group with ASD had significant relations in the N2 Go condition, $r(6) = .84$, $p = .04$ and the P3 Go condition, $r(6) = .82$, $p < .05$.

Conclusions: These results suggest that the N2 ERP response was more related within MZ than DZ twins with typical development. This is consistent with a stronger genetic contribution for task monitoring during the Go/No-Go task among typically developing twins. In contrast, among the twins with ASD the N2 ERP in Go condition was related within both MZ and DZ twin pairs. This suggests a stronger environmental contribution to performance among twins with ASD. Additional support for environmental influences on performance among the twin pairs with ASD was observed at the P3 component, which was more related in DZ twins. These results are intriguing as they are suggestive of a different pattern of factors that contribute to task monitoring and response preparation in twins with ASD as compared with TD. However, the sample size of this exploratory study is small, and replication will be essential.

**117.016 16** Atypical Connectivity of Default Mode and Salience Networks and Links with ASD Symptomatology. A. E. Abbott*[1], A. Nair[1], C. L. Keown[2], M. Datko[1], I. Fishman[3] and R. A. Müller[3], (1)*San Diego State University*, (2)*University of California San Diego*, (3)*Dept. of Psychology, San Diego State University*

Background: Recent findings from functional connectivity MRI studies suggest that typical brain functioning can be characterized by differentiation and integration of brain networks. However, in autism spectrum disorders (ASD), network dynamics appear impaired. Specifically, connectivity within functional networks appears reduced while connectivity between regions belonging to separate networks appears increased. Such inefficient network organization may particularly affect connectivity for primary nodes or hubs of major functional networks, such as the default mode network (DMN) and salience network (SN). Both networks have shown abnormalities in ASD and may be associated with characteristics of the disorder.

Objectives: To examine the functional connectivity of DMN and SN in relation to symptom severity in children with ASD.

Methods: Resting state fMRI data and behavioral measures (Social Responsiveness Scale [SRS], Sensory Profile [SP], and Repetitive Behavior Scale-Revised; RBS-R) were used to assess functioning in 34 ASD group and 31 matched TD participants (ages 7-17 years). FMRI data preprocessing was performed using AFNI and FSL. Data were slice-time, motion, and field map corrected. Functional data were co-registered onto the anatomical image and standardized into MNI space. Spatial smoothing at 6mm FWHM and bandpass filtering ($.008 < f < .08$ Hz) were applied. Time points with >1mm motion were censored and nuisance regressors removed, included 6 motion, physiological (heart rate and respiration), white matter, and ventricular time series and their derivatives. Regions of interest included two nodes in the SN (anterior insula, dorsal anterior cingulate cortex) and two nodes in

the DMN (posterior cingulate, medial prefrontal cortex). Time series for each nodes as well as for combined network nodes were correlated with time series from every other voxel in the brain. Additionally, time series for each network were correlated with one another to assess between network connectivity. Connectivity values (z') were correlated with behavioral measures within the ASD group.

Results: For the DMN, decreased connectivity in the ASD group was found with other regions implicated in DMN functioning, while increased connectivity was found with non-DMN regions. The SN showed reduced connectivity in the ASD group with the anterior prefrontal cortex bilaterally, which has been implicated in higher-order salience processing. Within the ASD group, connectivity between DMN and SN correlated negatively with behavioral scores from the SRS-Cognition subscale ($r(33) = -.567$, $p < .001$), i.e., symptomatic behaviors decreased with increasing connectivity.

Conclusions: Consistent with previous findings, we found reduced network integration (reduced within-network connectivity) in ASD for both DMN and SN, as well as reduced network differentiation (atypically increased out-of-network connectivity) for the DMN. However, the correlation between reduced symptom severity and increased cross-network (DMN-SN) connectivity suggests that between network connectivity may also be functional beneficial (or compensatory) for some networks in ASD.

**117.017 17** Causal Underpinnings of Sensory Hypersensitivities in Autism. M. M. Kjelgaard*[1], T. K. Gandhi[2], K. Tsourides[3], D. Pantazis[3] and P. Sinha[3], (1)*MGH Institute of Health Profesions*, (2)*Defence Institute of Physiology and Allied Sciences*, (3)*MIT*

Background:

Sensory hypersensitivities are diagnostic of autism spectrum disorder (ASD). Estimates are that 88% of individuals with ASD experience sensory hypersensitivities, the most common being auditory. We posit that impaired neural habituation may be a causal factor. Habituation to repeated sensory stimuli frees cognitive resources to process new information. Impairments in habituation would make for a confusing situation in which all sensory elements would be treated as equally salient. If one's ability to discount even highly repetitive sensory streams were impaired, the overwhelming sensory bombardment may manifest as a need to avoid further stimulation.

We studied habituation to auditory stimuli in children and young adults with ASD using two distinct measures of sensory sensitivity, one peripheral, galvanic skin response (GSR) and one central, magnetoencephalography (MEG).

Objectives:

To determine whether auditory habituation is impaired in ASD using GSR and MEG.

Methods:

GSR

Participants were 18 ASD and 20 age-matched NT controls. Electrodermal responses were recorded using Flexcomp Infinity™ encoder with a sampling rate of 2048 Hz. Two Ag-AgCl electrodes approximately 3 cms apart were attached to the palm of the non-dominant hand. Participants sat in a quiet room for baseline measurement and then listened to discrete beeps (1KHz, 73dB, beep duration=0.116s), with 1 second ISI for 5 minutes.

MEG

Participants were 14 ASD, 4 ASD siblings, and 5 age-matched NT controls. A metronomic sequence of 300 auditory beeps was presented. MEG signals were recorded from 306 channels (Elektra Neuromag TRIUX) at a sampling rate of 1000Hz, band-pass filtered between 0.03 and 330Hz. Auditory responses were obtained from MEG sensors near auditory cortices. Two auditory evoked response fields (ERFs) were computed by averaging 600ms signal fragments corresponding to the first and last 50 trials.

Results:

GSR

NT participants showed a decline in GSR prior to the onset of the tones as well as during the tone sequence; the onset of the tones elicited a transient response followed by a sustained decline. ASD participants, however, showed an increase in GSR during the tone sequence. The

slopes of GSR traces were calculated and group differences were significant. These analyses revealed negative slopes for NTs but positive ones for ASD. The difference between the average GSR amplitude during the first and last 60 seconds of the auditory presentations were also significant. ASD participants showed a significant increase in GSR amplitude over time, further evidence of reduced habituation.

MEG

NT participants showed marked habituation over the course of the auditory sequence; ERFs evoked by the impulses in the initial section of the auditory train were stronger than those evoked by the later ones. By contrast, the amplitude of auditory evoked responses in ASD participants consistently increased over time, resulting in stronger magnetic deflections during the final 50 trials relative to the first 50 trials, indicating a lack of habituation.

Conclusions:

ASD symptomology involves impaired habituation. Two distinct measures of sensitivity to auditory stimuli, GSR and MEG, revealed that while NT individuals habituated to tones, ASD did not. The findings have widespread implications for ASD clinical symptomology.

**117.018 18** Hubs of Functional Brain Networks Are Atypically Organized in Children with Autism. K. Supekar* and V. Menon, *Stanford University*

**Background:**

Hubs are uniquely situated brain regions that play a critical role in integrating modality-independent information across distributed brain networks. Remarkably, very little is currently known about the anatomical location as well as the functional organization of these hubs in autism spectrum disorder (ASD). Such knowledge is critical for understanding the brain's information processing architecture underlying cognitive dysfunction in ASD.

**Objectives:**

To characterize hubs of functional brain networks in children with ASD, and compare their features in terms of anatomical location as well as functional connections with the ones characterizing the typical developing brain.

**Methods:**

One cohort of 40 children (ASD = 20, age: 9.9±1.6; TD = 20, age: 9.9±1.6) was recruited at Stanford University, and a second cohort of 40 children (ASD = 20, age: 11.04±1.3; TD = 20, age: 10.83±1.6) was recruited at Georgetown University. Task-free fMRI were acquired from both cohorts.

Preprocessed fMRI datasets were parcellated into 264 cortical and subcortical regions using previously published functional templates. Correlation analysis of the extracted regional fMRI-time series was used to compute whole-brain inter-regional functional connectivity. Graph-analytical methods were used to identify putative hubs in the whole-brain functional connectivity networks. Specifically, *participation coefficient* - a network-measure of number of functional systems a region participates - was computed for each brain region. Using this metric, a hub was identified as a brain region with a high participation index thereby allowing the region to facilitate interactions between distributed functional systems. Critically, identification of hubs using participation coefficient overcomes the limitations of conventional degree-based hub identification techniques. Finally, to investigate how ASD pathology affects hub organization, we compare participation coefficient of each brain region between the ASD and TD group.

**Results:**

We examined the participation coefficient values obtained for the whole-brain functional connectivity network of each participant. In the Stanford cohort, the ASD group, compared to the TD group, showed smaller participation coefficient values for multiple brain regions including the right insula, right lateral occipital cortex/fusiform gyrus (LOC/FG), right superior temporal gyrus, and postcentral gyrus. Higher participant coefficient values in the ASD group, compared to the TD group, were observed for the posterior cingulate cortex. We repeated our entire analysis on the second group of children from the Georgetown cohort. Remarkably, in spite of differences in scanner (GE vs. Siemens), fMRI pulse sequence (spiral in-out vs. echo planar imaging) and other data acquisition protocols, results from the Georgetown cohort replicated the Stanford-cohort finding of atypical hub

organization in children with ASD. Specifically, in the Georgetown cohort, the right insula and the right LOC/FG – key nodes of the salience and face processing systems - showed smaller participation coefficients in the ASD group, compared to the TD group.

**Conclusions:**

Our findings provide robust evidence for atypical organization of hubs in childhood autism, particularly those situated in brain systems critical for attention to salient stimuli and face processing. We propose that dysfunctional hubs may lead to impaired signaling between brain systems important for processing salient socially-relevant stimuli, potentially resulting in social deficits among children with ASD.

**117.019 19** Precuneus Hyper-Perfusion Relates to Symptom Severity and Hypoconnectivity in Individuals with Autism Spectrum Disorder. E. Kilroy*[1], K. Jann[2], D. Beck-Pancer[2], L. M. Hernandez[3], D. J. Wang[2] and M. Dapretto[3], (1)*University of Southern California*, (2)*UCLA*, (3)*University of California, Los Angeles*

Background: Social deficitits in Autism Spectrum Disorder (ASD) have been associated with abberrant patterns of blood oxygenation level dependent (BOLD) resting state functional connectivity MRI (rs-fcMRI**)** (Fair, 2007; Assaf, 2010). More recent work has used Arterial Spin Labeled (ASL) perfusion MRI to assess functional connectivity by quantifying cerebral blood flow (CBF), which is inaccessible to conventional BOLD. Comparisons of CBF in resting state networks in ASD and TD individuals may elucidate mechanisms of network dysfunction in ASD. To our knowledge, no study to date has investigated perfusion-based resting state networks in ASD.

Objectives: This study aims to explore differences in CBF-based functional connectivity in ASD and TD individuals, and how these differences may be related to severity of social symptoms assessed with the Social Responsiveness Scale (SRS; Constantino, 2003).

Methods: Eleven high-functioning children and adolescents with ASD (age [years] mean±SD: 12.93±0.95; 4 unmedicated, 3 female) and eleven typically developing (TD) participants (13.73±3.42, 1 female) were recruited. MRI data was collected on a 3-T Siemens Trio Scanner. The imaging protocol included a T1-weighted structural MRI and resting-state background-suppressed 3D GRASE pseudo continuous ASL (Fernandez-Seara, 2008). Standard preprocessing and CBF quantification were performed. Data were restricted to grey-matter voxels and zero-meaned before subjected to a Group ICA using GIFT (Calhoun, 2001). ICA model order was determined using the AIC/MDL criterion. The default mode network (DMN) was identified using GIFT component labeller and visual inspection. $DMN_{CBF}$was extracted at z-threshold>2 from each participant, controlling for globalCBF and total intracranial volume. Multiple regression analyses were performed on the TD and ASD groups together and separately. SRS scores were correlated with average baseline perfusion controlling for age, sex and global CBF. Moreover, these regional CBF values were correlated to functional connectivity maps.

Results: ASD and TD participants showed highly similar DMNs; however, differences were observed in the posteromedial cortex (dorsal precuneus), where individuals with ASD showed reduced connectivity compared to TD individuals. Furthermore, in the ASD group, SRS scores were positively correlated with CBF rs-fcMRI in the dorsal precuneus such that greater social impairment was related to increased CBF ($p<$ 0.01; t(6)=3.14). CBF values from the precuneus ROI were also positively correlated with SRS total score in ASD (r=.856, $p<.007$). Moreover, voxel-wise correlation of the precuneus ROI CBF values with individual ASD functional connectivity maps revealed a widespread reduction of DMN connectivity with increased precuneus CBF.

Conclusions: Our results support previous findings of precuneus hypoconnectivity in ASD, and a relationship to social behavior (Lynch, 2013). The relationship between social deficits and CBF in the precuneus suggests dysfunctional hyperactivity in this area in ASD. Decreased connectivity has been observed in ASD between the precuneus and the dorsal lateral and medial prefrontal cortex, regions relevant for social processing and executive/memory functions, where individuals with ASD typically show deficits (Kennedy, 2008). Taken together, our results suggest that hyperperfusion in this area might lead to altered rs-fcMRI and highlight the need to investigate underlying neuro-physiological differences in ASD.

**117.020 20** DNA Methylation of the Oxytocin Receptor Gene As a Predictor of Social Brain Function in Families with ASD. A. Jack*[1], K. A. Pelphrey[1], C. Keifer[1], J. P. Morris[2] and J. J. Connelly[2], (1)*Yale University*, (2)*University of Virginia*

Background:

Oxytocin (OXT) is a sexually dimorphic hormone associated with important social perceptual and affiliative processes[1–6]—processes known to to be impacted in ASD. Moreover, OXT levels may be depressed in ASD[7], and recent work demonstrates that OXT administration to persons with ASD is associated with a more "neurotypical" brain response to social stimuli.

OXT's action is mediated in humans via the oxytocin receptor (OXTR)[8]. Several genetic variants of *OXTR* have been associated with autism spectrum disorders[9–12]. However, the function of *OXTR* is likely to be affected not just by genetic variation but also by epigenetic factors—that is, modifications to chromatin that regulate gene expression. Important preliminary research suggests that DNA methylation (a form of epigenetic modification most commonly associated with transcriptional silencing) of *OXTR* could play a role in social functioning and ASD status. Specifically, degree of *OXTR* methylation has been associated with variability in social brain function in health adults[13] and increased *OXTR* methylation is associated with presence of ASD[14].

This evidence suggests that an investigation of *OXTR* methylation and its relation to ASD symptoms and social brain function may be informative about ASD etiology. Additionally, the sexually dimorphic action of OXT makes it worthwhile to examine whether and how these relationships vary by gender.

Objectives:

- Characterize relationships among *OXTR* methylation, social behavior, and social brain function for individuals with ASD and their families
- Investigate whether and how these relationship vary as a function of gender

Methods:

We leverage the unique characteristics of an ACE network focused on the multimodal assessment of girls with ASD to recruit deeply-phenotyped girls and boys with ASD and their families. All family members provide samples of whole blood from which mononuclear cell DNA is isolated for *OXTR* methylation analysis. Children with ASD and their unaffected siblings additionally participate in fMRI paradigms focused on processes of both lower- (point-light displays of biological motion) and higher-order (Heider & Simmel[15] animations) social perception. Percent *OXTR* methylation is included as the regressor of interest in analyses of fMRI data to determine regions in which methylation is related to social brain response.

Results:

To date we have collected usable blood and fMRI data from 4 affected families (parents, probands, and unaffected siblings) as well as 5 control families. We hypothesize that 1) individuals with ASD will display a higher level of *OXTR* methylation, on average, than either their unaffected relatives or typically developing controls; 2) unaffected siblings will display a positive relationship between social brain activity and *OXTR* methylation, indicating a compensatory response; 3) individuals with ASD will display a negative or attentuated relationship between social brain activity and *OXTR* methylation; and 4) these relationships will be stronger for males than females.

Conclusions:

This is the first study to examine the relationship between *OXTR* methylation and social brain function among individuals with ASD. Understanding the contribution of epigenetic factors to neuroendophenotypes of ASD and gender differences in the disorder will advance our understanding of the etiology of ASD more broadly.

**117.021 21** Neural Responses to Biological Motion at 3 Months: A Functional Near-Infrared Spectroscopy (fNIRS) Study Comparing Infants at Low and High Risk for Autism. L. C. Anderson*[1], H. M. Fichtenholtz[2], N. M. McDonald[2], D. Z. Bolling[3] and K. A. Pelphrey[3], (1)*University of Maryland*, (2)*Child Study Center, Yale University*, (3)*Yale University*

**Background:** From birth, human infants preferentially attend to point-light displays (PLDs) of biological motion over scrambled motion (Simion, Regolin, & Bulf, 2008), suggesting an evolutionarily conserved mechanism to support

social engagement. The network of brain regions involved in biological motion processing—including the posterior superior temporal sulcus (pSTS)—consistently shows dysfunction in autism as compared to typical development. The early development of this neural system, however, is not well understood, in part because of practical difficulties in the neuroimaging of awake infants. Functional near-infrared spectroscopy (fNIRS) is well-suited to overcome these limitations. Recent work (Lloyd-Fox et al., 2013) has demonstrated that 4- to 6-month-old infants at high risk for autism show less selective neural responses to biological motion than low-risk infants, however it is unclear whether these differences are present in the first 3 months of life. Examining the early neural correlates of biological motion processing could elucidate the brain bases of ASD.

**Objectives:** We examined the neural underpinnings of biological motion processing at 3 months of age to determine whether neural differences exist in infants who are at high risk (HR) versus low risk (LR) for ASD at this early age.

**Methods:** Infants were defined as high-risk if they had an older sibling with autism. We monitored regional cerebral blood oxygenation changes using a 24-channel NIRS apparatus over bilateral temporal cortex to investigate brain activity while infants viewed 10s video clips of biological and scrambled motion PLDs. Infants were video-recorded so that looking time could be assessed offline, frame-by-frame. Preprocessing included low- (0.7 Hz) and high-pass (0.01 Hz) filtering, and exclusion of trials containing evidence of excessive motion and/or looking time of less than 75 percent.

To date, participants include 6 LR infants and 5 HR infants, matched on age (LR: $M$ = 3.42 months, $SD$ = 0.52; HR: $M$ = 3.53 months, $SD$ = 0.47). We calculated changes in oxy-Hb in each recording channel for integrated blocks of biological and scrambled trials. We then averaged measurements for each hemisphere separately to obtain waveforms representing the infants' neural response to biological and scrambled motion in left and right temporal regions.

**Results:** In the right temporal region, the differential response to biological versus scrambled motion was marginally greater in LR infants between 7–10 seconds post-stimulus onset ($t(9) = 1.75$, $p = 0.11$). Interestingly, this difference between LR and HR infants was driven by a deactivation to scrambled motion in the low-risk infants. We expect these findings to reach significance with a larger sample.

**Conclusions:** These findings suggest that the neural mechanisms for processing biological motion are present in the first 3 months of life in typical development and show atypical patterns in infants at risk for autism by 3 months. Although only a fraction of the HR infants will go on to develop autism, lack of differentiation between biological and scrambled motion in this group may represent a neuroendophenotype or genetic liability to develop autism, which, crucially, is present prior to the onset of clear behavioral symptoms.

**117.022 22** 'Reading the Mind in the Eyes': Phenotypic and Endophenotypic Associations in Males and Females with Autism. R. Holt*[1], L. R. Chura[2], M. C. Lai[2], J. Suckling[2], E. von dem Hagen[3], A. Calder[3], E. Bullmore[2], S. Baron-Cohen[2] and M. D. Spencer[2], (1)*Autism Research Centre, University of Cambridge*, (2)*University of Cambridge*, (3)*MRC Cognition and Brain Sciences Unit*

Background: Atypical social cognitive processing is a hallmark of autism spectrum conditions (ASC), and a potential endophenotype for ASC. Endophenotypes are heritable components associated with increased risk for a condition that are apparent in family members at a higher rate than the general population, independent of whether the family member has the condition or not (Gottesman & Gould, 2003). Differences in performance and neural activation on the 'Reading the Mind in the Eyes' (Eyes task) have been identified in individuals with ASC compared to neurotypical individuals in previous studies.

Objectives: This study aimed to examine group differences (ASC vs. controls and siblings vs. controls) in performance and neural activation on the Eyes task, to establish whether they are potential phenotypic or endophenotypic markers for autism.

Methods: Performance on the Eyes task and the associated neural activation was examined in adolescents (aged 12-18 years) with ASC (N=50), their unaffected related siblings (N=40) and typically developing controls (N=40). Because the prior literature suggests that males and females

with ASC may display different cognitive and associated neural characteristics, analyses were stratified by sex. Three strategies were applied to test for endophenotype at the level of neural activation: (1) identifying and locating conjunctions of ASC-control and sibling-control differences; (2) examining whether the sibling group is comparable to the ASC or intermediate between the ASC and control groups; and (3) examining spatial overlaps between ASC-control and sibling-control differences across multiple thresholds.

Results: Performance differences on the task were observed in male participants ($F(2, 61)=3.39$, $p=0.04$), where impaired performance on the Eyes task was observed in the ASC compared to the control groups ($p=0.016$). In females, only trend level group differences were observed between the ASC and control groups ($p=0.051$). In either sex, no performance difference was identified between sibling and same-sex control groups. In males, task-related increase in neural activation was observed in the control compared to the ASC groups in a left lateralized cluster (FDR $q=0.004$; cluster size Ke=2263; peak-coordinate MNI=-36, 36, -8) involving the inferior prefrontal cortex, orbitofrontal, temporopolar and middle temporal gyrus. In females there was also significantly greater activation in the control compared to the ASC groups in a cluster (FDR $q=0.017$; Ke=2661; peak-coordinate MNI=14 24 6) involving bilateral inferior prefrontal gyrus, left orbitofrontal and left anterior prefrontal cortex. Most importantly, neural activation showed a significant and substantial endophenotypic effect in the female groups (in the direction of [control>ASC AND control>siblings]), but only modest in the male groups.

Conclusions: Behavioural impairment on complex emotion recognition associated with mental state attribution is a phenotypic, rather than endophenotypic marker of ASC. The neural response to the Eyes task may serve as a potential endophenotypic marker for ASC, particularly in females. These findings contribute to the understanding of the neural mechanism underlying social cognition in autism, indicating a possible genetic basis to the associated neural response.

**117.023 23** Premotor Potential Differences in Autism Spectrum Disorder, ADHD and Neurotypical Children. M. F. Casanova*[1], S. M. Edelson[2], L. L. Sears[1] and E. M. Sokhadze[1], (1)*University of Louisville*, (2)*Autism Research Institute*

Background:

Motor abnormalities in autism bear the characteristics of precedence and universality that characterize a core symptom. Underlying the motor skill deficits in autism and Asperger syndrome is a dyspraxia that by definition is an inability to plan, organize, and execute movements in the absence of any known physical and/or neurological condition. This deficit is more apparent in autism spectrum disorders when compared to other neurodevelopmental disabilities, i.e., ADHD.

Objectives:

The lateralized readiness potential (LRP) is an index of motor processes and it is assumed that this brain potential is generated by a source within the motor cortex. LRP reflects the response-specific involvement of the left and right cortices of the brain and enables the determination of the point in time at which the activation of the motor cortex controlling one hand surpasses the activation of the motor cortex controlling the other side. The LRP is assumed to be related to selective response activation. It captures the asymmetric portion of the late Bereitschaftspotential (BP) preceding hand or foot movements. It is important for the mental chronometry that LRP helps to determine the exact point in time when sensory information affects motor processing and response execution.

Methods:

Our goal was to compare differences in LRP during cued spatial attention task between group of children with Autism Spectrum Disorder (ASD), Attention Deficit Hyperactivity Disorder (ADHD), and neurotypical (NT) children (N=12/group, mean age 14.6 years). Each study participant performed a Posner spatial attention task with congruent (correctly cued, 75%) and incongruent (incorrectly cued, 25%) trials with dense-array EEG recording (128 channel Electrical Geodesics Inc. EEG system). In our study we used stimulus-locked LRP method of waveform calculation and since S1-S2 interval was set on 1s, we computed

mean LRP (in uV) and integrated LRP values for 2 windows (early 600-800 ms post S1 stimulus; and late – 800-1200 ms post-stimulus components of LRP).

Results:

In our sample of ASD, ADHD and NT controls, differences were not significant at the early stage, but became significant at the late stage of the LRP yielding significant *Time* (early, late) X *Group* interaction (F=6.77, p=0.012). Post-hoc analysis showed group differences at 1000-1200 ms post stimulus window (F=4.81, p=0.033) between autism and control groups. Autism group also showed more pronounced differences of LRPs in incongruent trials as compared with both ADHD and NT groups.

Conclusions: Our study showed suggests more deficient motor preparation during tasks congruency manipulations in children with ASD as compared to ADHD and neurotypicals manifested in LRP components reflective of abnormal motor preparation processing.

**117.024 24** Analysis of Temporal Dynamics of Brain Functional Connectivity in Autism. Y. Ghanbari*[1], L. Bloy[2], V. Shankar[1], J. C. Edgar[2], R. T. Schultz[3], T. P. Roberts[2] and R. Verma[1], (1)*University of Pennsylvania*, (2)*Children's Hospital of Philadelphia*, (3)*The Children's Hospital of Philadelphia*

Background: There is increasing evidence that autism spectrum disorder (ASD) is associated with disruptions in the excitatory/inhibitory balance of neural activity leading to abnormal functional connectivity of the brain, thereby causing inefficient information processing. Examination of oscillatory resting-state MEG activity within specific frequency bands affords insight into these brain abnormalities. Amongst these frequency bands, recent studies have demonstrated delta-band (1–4 Hz) connectivity alterations in ASD, with the connectivity being computed over large time intervals. However, analysis of resting-state brain connectivity dynamics in short-time windows may provide a greater insight into the differential effect of ASD pathology.

Objectives: The aim of this work is to investigate difference in temporal connectivity dynamics of the resting-state MEG source-space signal, between ASD and typically developing control (TDC), with connectivity computed in short-time windows in the delta band. Connectivity is characterized using network measures of modularity, clustering coefficient, long/short-range connectivity ratio and connectivity entropy.

Methods: Resting-state MEG eyes-closed data was collected on 27 ASD (aged 6.4 – 13.6 years) and 27 TDC (aged 6.1 – 13.9 years) age-matched children ($p>0.8$) using a 306-channel Elekta machine. The data was band-pass filtered to the delta band and mapped into the frequency domain using Fourier transforms. Sensor-to-source space mapping was done using VESTAL to obtain densely sampled source time-courses. 100-sec source signals, obtained after artifact removal, were segmented into 10-sec courses with 5-sec overlap, yielding 19 segments. Functional connectivity at each segment was quantified using time-frequency synchronization likelihood (SL) yielding a symmetric matrix. Network measures of modularity, clustering coefficient, long/short-range connectivity ratio and Von Neumann matrix entropy were computed for these 19 matrices per subject. Group differences were analyzed via t-tests at each of 19 time instants.

Results: The temporal connectivity dynamics showed differences between ASD and TDCs. Specifically, increased modularity in ASD versus TDC was observed in over 70% of time instances ($p<0.05$). In contrast, the clustering coefficient was consistently higher in TDC with high significance in one third of time instances ($p<0.05$). The ratio of long- over short-range connections was higher in TDC, with significance in over half of the time instances ($p<0.05$). The connectivity matrix entropy had a greater differentiating power compared to traditional global network measures, with ASD displaying higher entropy in 100% of time instances ($p<0.001$).

Conclusions: This study of temporal connectivity dynamics of resting-state MEG data demonstrated increased network modularity and decreased clustering coefficient in ASD. This is indicative of ASD being inconsistent with the small-world network structure. The decrease in long/short-range connectivity ratio in ASD demonstrates that ASD suffers from an imbalance in the proportion of long- and short-range connections, with short-range connectivity dominating. Finally, the increased matrix entropy in ASD may be indicative of a disorganized brain network, which perhaps leads to less regulation of neural activity.

This study highlights the need for quantifying the temporally changing connectivity patterns of MEG data, so that the subtle changes induced by pathology can be appropriately characterized.

**117.025 25** fMRI Imaging Results for Adolescents Who Received Treatment for Autism As Preschoolers. T. D. Graupner*[1], G. O. Sallows[1] and R. J. Davidson[2], (1)*Wisconsin Early Autism Project*, (2)*Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin*

Background:
Numerous studies have found that a large proportion of children with autism show significant gains in cognitive, social, language and academic skills following early intensive behavioral therapy. It has also been found that due to processes underlying brain plasticity, learning and practicing new skills results in growth of new synapses in the brain and improved connectivity in typically developing adults and children. However, there has been little information on whether behavioral improvement resulting from intensive behavioral treatment is reflected in normalized brain functioning within structures known to be abnormal in autism.

Objectives:
This study aimed to determine whether behavioral gains and improved test scores following intensive behavioral treatment would be reflected in changes in brain functioning. It was hypothesized that adolescents diagnosed with autism as preschoolers, who demonstrated large improvement during intensive behavioral treatment (Rapid Learners), would show patterns of brain activation similar to that of typically developing adolescents. In contrast, it was hypothesized that adolescents diagnosed with autism as preschoolers, who demonstrated more modest gains during treatment (Moderate Learners), as well as untreated high functioning adolescents with autism, would continue to show aberrant patterns of brain activation similar to that described in studies of individuals with autism.

Methods:
Follow up data was collected at age 16 for 15 adolescents who had participated in intensive behavioral treatment for autism when they were 3 to 7 years old. Ten of the 15 had shown large gains to the average range. Eleven untreated high functioning adolescents with autism and six typically developing adolescents served as controls. All groups were matched on age and IQ. Participants were scanned during a facial emotion recognition task to examine patterns of activation in the fusiform gyrus and amygdala. Several previous studies of autistic adolescents had found abnormal activation in these areas during this task. FMRI was also used to examine activation in occipital and frontal areas, which have been implicated in aberrant brain activation in autism during face processing. DTI data were obtained during resting state scans to examine issues related to connectivity, which has been found to be atypical in autism.

Results:
Adolescents who had shown dramatic improvement to the average range on test scores during treatment (Rapid Learners) showed patterns of brain activation and DTI values that were similar to those of typically developing adolescents. Adolescents who had shown less robust response to treatment (Moderate Learners), as well as the group of untreated autistic adolescents with average IQs, showed aberrant brain activation patterns characteristic of individuals with autism. Summarizing, Rapid Learners were similar to typically developing adolescents, but different from Moderate Learners and different from untreated high functioning adolescents with autism.

Conclusions:
Although the sample size was small, these findings suggest a trend toward supporting the hypothesis that early intensive behavioral treatment and processes underlying brain plasticity, may result in remediation of abnormal brain functioning, at least for children who show large improvements during treatment.

**117.026 26** Human Versus Non-Human Action Sound Processing in Young Children with Autism. C. Stefanidou*[1], R. Ceponiene[2] and J. P. McCleery[3], (1)*School of Psychology, University of Birmingham*, (2)*UCSD Medical Center*, (3)*University of Birmingham*

Background: Autism spectrum disorders (ASDs) are characterized by difficulties in communication and social interaction, including the comprehension of non-verbal behaviours such as other people's actions and gestures. Behavioural and neuroimaging studies have revealed reduced attention to social cues, such as eye-gaze or gestures, as well as atypical visual perceptual processing of biological motion and human actions

in this population. However, it is not known whether atypical neural activity is confined to the perceptual processing of visual social stimuli or, instead, extends to social perception in the auditory modality.

Objectives: The aim of the current study was to examine the perceptual processing of human and non-human action-related sounds in 4- to 6-year old high-functioning children with ASD compared with typically developing control children, matched for sex, chronological age, and verbal abilities.

Methods: An auditory-auditory repetition suppression event-related potentials (ERPs) paradigm was employed, whereby children with ASD (n=18) and typically developing controls (n=18) passively listened to repeated and non-repeated human action or environmental sound stimuli. More specifically, the ERP paradigm included a single block of trials, presenting two types of human action sounds (hands clapping, hands ripping paper) and two types of non-human action sounds (helicopter blades spinning, ocean waves). There were four different types of trials, which involved the immediate repetition or non-repetition of human and non-human action sound stimuli. Differences in neural activity elicited by repeated (suppression of brain mechanisms) and non-repeated (release of brain mechanisms) stimuli were examined. Behavioural measures, including the Mullen Scales of Early Learning and the Autism Diagnostic Observation Schedule, were also administered for the behavioural characterisation and matching of the participant groups.

Results: ERPs to both types of sounds included early sensory (P1, N1) and later cognitive processing components (N4, N600) over both frontal and temporal sites, which did not differ between the participant groups. However, children with ASD presented with enhanced cortical responses to the non-human action sounds over posterior parietal sites at an early stage of perceptual/cognitive processing (N2b), when compared with controls. In addition, children with autism exhibited less habituation to human action sounds relative to controls, at a later stage of cognitive processing (N4) over the same parietal electrode sites.

Conclusions: The current results provide evidence for atypical processing of both human and non-human action sounds in young children with autism. These results are consistent with previous findings of atypical visual perceptual processing of objects in young children with autism, and suggest that similar atypicalities exist in the auditory and visual domains. The finding of reduced habituation to human action sounds in the current study is also consistent with recent findings of both visual and auditory social processing in this population early in life. Taken together, the current results provide further evidence for an imbalance between social and non-social processing mechanisms in young children with autism.

**117.027 27** Wake EEG Coherence before and after Sleep in Adults with Autism: Decreased Morning Frontal Connectivity. C. Léveillé[1], E. Chevrier[1], L. Mottron[2] and R. Godbout*[3], (1)*Sleep Laboratory & Clinic, Hop. Riviere-des-Prairies*, (2)*Centre de Recherche de l'Institut Universitaire de Santé Mentale de Montréal*, (3)*Sleep Laboratory & Clinic, Hop. Riviere-des-Prairies, Universite de Montreal*

Background: Autism is a neurodeveloppemental disorder characterized by atypical connectivity between brain regions. People with autism are known to have sleep disorders.

Objectives: The purpose of this study was to analyze brain connectivity before and after a night of sleep using EEG coherence analysis.

Methods: Nine adults with autism (21.1 ± 4.0 years) and 20 control participants (20.8 ± 4.2 years) were recorded for two consecutive nights in a sleep laboratory, using a 22-electrode montage. Every participant had a normal IQ and none were taking medication. Wake EEG was recorded for 5 minutes at bedtime and just before final rise time in the morning, while lying in bed with eyes closed. EEG coherence values were compared with a multivariate repeated measures design using Group x Moment x Frequency band factors for each electrode separately, followed by post hoc tests.

Results: In the evening, the autistic group displayed **more** Alpha coherence than controls within the left visual area (P3-O1: p=0.049; T5-O1: p=0.03 and T5-P3: p=0.014). In the morning more Alpha coherence in the autistic group within the left visual area was also measured (T5-O1: p=0.009 and T5-P3: p=0.015) as well as **more**

Delta coherence at the T5-O1 electrode pair (p=.027). Moreover, morning recordings showed **less** Delta coherence within the right frontal area, (Fp2-F8: p=0.037; F4-F8: p=0.011) and between left and right hemispheres (F3-F4: p=0.019; F7-F8: p=0.003).

Conclusions: A previous study performed during REM sleep (Léveillé et al., 2010) found a greater intrahemispheric EEG coherence in autistic participants compared to controls between the left visual cortex and regions either close to or distant from it. The present results are in the same direction, upon both evening and morning wake recordings, suggesting that sleep per se is not responsible for these signs of overconnectivity. The present results also revealed a morning specific lower EEG coherence values for slow frequencies in the right frontal area in participants with autism compared to controls, suggesting that sleep per se could be responsible for these signs of underconnectivity.

**117.028 28** Attention Networks and Sociocommunicative Abilities in ASD: Functional Connectivity and Behavioral Performance. M. Ghane*[1], B. Keehn[2], A. Nair[3], A. Abbott[1], C. L. Keown[3], J. A. Richey[4], J. Townsend[5] and R. A. Müller[1], (1)*San Diego State University*, (2)*Children's Hospital Boston*, (3)*University of California San Diego*, (4)*Virginia Tech*, (5)*University of California, San Diego*

Background:

Attentional abnormalities, as documented in numerous studies of Autism Spectrum Disorders (ASD), are potential contributors to the emergence of socio-communicative deficits. According to Posner and colleagues (2004), attention is organized into three functionally separate but interrelated networks: alerting, orienting, and executive. Atypical attention function in ASD has been shown for specific attention networks using electroencephalography, functional magnetic resonance imaging, and functional connectivity MRI (fcMRI).

Objectives:

We used resting-state fcMRI and the modified Attention Network Test (mANT) to characterize the organization and efficiency of attention networks and their relationship to socio-communicative deficits in ASD. We predicted that in adolescents with ASD: functional-connectivity would be reduced within each attentional network, but atypically increased between networks (reflecting reduced independence of attention networks); attention modulation would be inefficient; and atypical connectivity and network modulation would be associated with socio-communication symptom severity.

Methods:

The imaging study included 20 adolescents with ASD and 20 matched typically developing (TD) individuals. Imaging analyses explored seed-based connectivity within and between attention network regions, as well as between each network and the whole brain. The mANT was used in a subsample (n=14 ASD; 18 TD) to examine network efficiency and modulation. Main effects and interactions between conditions were assessed using the median response times of all correct trials entered into a 2(Group)x2(Alerting Tone)x2(Orienting Cue)x2(Congruency)x2(Stimulus-Onset-Asynchrony) mixed-model ANOVA. T-tests were conducted to test the interaction between network scores. Network and region specific fc-indices and mANT scores for individual networks were correlated with measures of socio-communicative functioning, including the Autism Diagnostic Observation Schedule (ADOS).

Results:

While no group difference was found for within and between network connectivity (*ps*>.05), significant differences were detected for whole-brain connectivity of each network, i.e., for connectivity with regions outside attentional networks (*ps*<.05). These differences were characterized by underconnectivity in the ASD group between the alerting network and cerebellum and somatosensory cortex, between the orienting network and parietal and somatosensory cortex, and between the executive network and superior parietal regions. Overconnectivity in the ASD group was detected between the alerting network and parietal regions, as well as the orienting network and frontal, superior parietal, temporal, and cerebellar regions.

MANT results showed a significant two-way interaction for orienting cue by group ($F_{(2,50)}$=3.813, p=.029), and a significant three-way interaction for orienting cue by executive

congruency by group ($F_{(2,50)}$=3.280, p=.046). As a whole, the ASD group showed less efficient patterns of attention network function and interaction.

Correlations between network scores on the mANT and between network fc-indices showed reduced independence of attention networks in the ASD compared to TD group. There were significant correlations in ASD between alerting and orienting network scores and the ADOS Social and Total scores. Also, executive network fc-indices showed correlations with ADOS Communication scores. Greater ASD symptom severity is associated with reduced attention network efficiency.

Conclusions:

Our findings support inefficient attentional function at the neural and behavioral levels in ASD. Atypical attentional function and organization were related to socio-communicative abilities suggesting a role in autism symptomatology.

**117.029 29** The Relationship Between Resting-State Functional Connectivity Between Language Areas and Oral Comprehension in Children with Autism. S. D. Washington*[1], E. M. Gordon[2], J. Brar[1], W. D. Gaillard[3], M. L. Kalbfleisch[4] and J. W. VanMeter[1], (1)*Georgetown University Medical Center*, (2)*Georgetown University*, (3)*Children's National Medical Center*, (4)*George Mason University*

Background: Autism spectrum disorder (ASD) is characterized by socio-communication deficits, including receptive language deficits. Resting-state functional connectivity has been useful to the study of neural substrates of speech and language but has seldom been used to study receptive language deficits in children with ASD.

Objectives: To determine how resting state functional connectivity affects receptive language by comparing resting-state functional MRI between commonly-recognized anterior and posterior language areas with performance on Oral Comprehension subtest of the Woodcock Johnson Test of Cognitive Skills III (WJ3) in typically developing (TD) children and those with ASD.

Methods: Subjects were scanned during performance of the modified flanker task using an echo-planar imaging (EPI) sequence with the following parameters: TR = 3000ms, TE = 30ms, flip angle = 90°, matrix size = 64x64, FOV = 192x192mm$^2$, 50 slices with a thickness of 2.8mm and a 0.2mm gap for an effective resolution of 3.0x3.0x3.0mm$^3$. We obtained resting state data from our subjects by analyzing BOLD fluctuations associated with the fixation condition blocks of a modifier flanker task. There were a total of four fixation blocks (42 secs each) for a total non-task time of 3 minutes, 12 seconds. We measured functional connectivity between common cortical substrates of language areas and their right-hemispheric homologues using partial-correlation in 24 TD children and 24 children with ASD (ages 6-18). Subjects who exhibited large motion artifacts were excluded from all groups (ArtRepair: threshold of 10% of scans per subjects having > 1.5% average global whole volume signal change). Bilateral regions of interest (ROIs) included Brodmann's area (BA) 41+42 (Heschl's gyrus, including primary auditory cortex), anterior BA 22 (word-form area), posterior BA 22 (Wernicke's area), BA 44 (Broca's area, pars opercularis), and BA 45 (Broca's area, pars triangularis).

Results: Fifty-three percent (24/45) of the correlations comparing functional connectivity between ROIs and standardized WJ3 Oral Comprehension subtest scores in children with ASD were significant ($p < 0.05$), but none were significant in TD children. Seventy-one percent (17/24) of these connections were frontotemporal, and 29% were temporotemporal. Further, 50% of these connections were inter-hemispheric, 29% were intra-hemispheric on the left side, and 21% (5/24) were right intra-hemispheric on the right side. ROI-pairs that included left BA 41+42, right anterior BA 22, and left or right BA 44 correlated best with oral comprehension. Correlations were never greater in TD children than in children with ASD, and we statistically verified that differences between correlational coefficients in the TD and ASD groups were significant. Similar comparisons with other WJ3 subtests were not as robust. None of these findings extended to functional connectivity within the default mode network.

Conclusions: Resting state functional connectivity between language areas is a better predictor of oral comprehension in children with ASD than in TD children. The effect did not extend to the default mode network, indicating that this relationship is specific to the connectivity between cortical areas important for language. These

results illustrate that functional connectivity between language areas is a predictor of receptive language ability in children with ASD.

**117.030 30** Behavioral and Electrophysiological Evidence of Impaired Social Orienting in 'Unaffected' Siblings of Children with Autism Spectrum Disorder. B. Keehn*[1], J. Martin[1], S. Mumanachit[1], H. Tager-Flusberg[2] and C. A. Nelson[3], (1)*Boston Children's Hospital*, (2)*Boston University*, (3)*Harvard Medical School*

Background: Failure to respond to name and impaired orienting to both social and non-social information has previously been found in infants and children diagnosed with or at risk for autism spectrum disorder (ASD). Further, event-related potential (ERP) studies investigating selective attention have demonstrated reduced P3a amplitudes in individuals with ASD, which may be indicative of deficits in processing novel information and attentional capture in ASD.

Objectives: To investigate behavioral and electrophysiological indices of orienting to social and non-social information in high-risk children (defined as having an older sibling with ASD) with (HRA+) and without (HRA-) a diagnosis of ASD and low-risk typically developing (TD) children (defined as having a TD older sibling).

Methods: Data collection for the current project is ongoing. To date, participants are nine 4 to 5 year old HRA- and 10 age- and IQ-matched low-risk, TD children. The study consisted of separate behavioral orienting and auditory odd-ball ERP experiments. For the behavioral orienting paradigm (modeled after Dawson et al., 1998; 2004), one experimenter engaged the child's attention, while a second experimenter administered a series of 12 possible social or non-social sounds. Social sounds (hum, clap, laugh, yawn, snap, and the child's name) and non-social sounds (toy rattle, car horn, toy squeak, vacuum, referee whistle, and a phone ring) were equated in intensity (70 dB) and duration (approximately 1 second). Child's orienting behavior, defined by either a head movement or a gaze shift was coded online by experimenters. For the auditory odd-ball task, auditory stimuli were identical to those used in the behavioral orienting paradigm. EEG was recorded using 128-channel high-density Geodesic electrode arrays, sampled at 500 Hz, and referenced to single vertex electrode. Data were segmented into 1200ms epochs (200ms pre- and 1000ms post-stimulus onset), trial/artifact rejected, and re-referenced to average reference. Mean amplitude and latency of the P3a component was measured for both social and non-social sounds.

Results: Paired t-tests showed that TD children oriented more frequently to social compared to non-social sounds, $p < .01$; In contrast, HRA- children shifted attention to both social and non-social sound at similar rates, $p = .3$. Independent samples t-tests demonstrated that, compared to HRA- children, TD children shifted attention more frequently to social stimuli, $p < .01$, but not non-social stimuli, $p < .1$. Electrophysiological data revealed a similar pattern of results; for the TD group, there was a larger P3a response to social stimuli than to non-social sounds, $p < 0.05$. However, for the HRA- group there was no significant difference in P3a amplitude for social compared to non-social sounds, $p > 0.5$.

Conclusions: Behavioral and electrophysiological indices of orienting suggest social information is perceived as more salient and captures attention to a greater degree in TD but not HRA- children. Similar to prior findings of impaired social orienting in children with ASD, our preliminary results suggest that social orienting deficits may be present in clinically 'unaffected' siblings, and therefore represent a potential endophenotype.

**117.031 31** Abnormal Neural Correlates of Audiovisual Multisensory Integration in Autism Spectrum Disorders. L. Latterner*[1], J. Foss-Feig[2], A. P. F. Key[3], M. T. Wallace[3], W. L. Stone[4], R. L. Johnston[5] and J. McPartland[2], (1)*Yale Child Study Center*, (2)*Yale University*, (3)*Vanderbilt University*, (4)*University of Washington*, (5)*Vanderbilt University Medical Center*

Background: Individuals with autism spectrum disorders (ASD) exhibit abnormalities in multiple modalities of sensory functioning and in multisensory integration (Iarocci & McDonald, 2006; Rogers & Ozonoff, 2005). For example, utilizing a multisensory "flash-beep" illusion wherein presentation of a single visual flash along with two temporally proximal auditory beeps results in perception of an illusory second flash (Shams et al., 2000), research has revealed capacity for cross-modal integration in ASD (Van de Smagt et al, 2007), but an extended temporal window over which stimuli are integrated (Foss-Feig et al, 2010). Research using event-related potentials (ERP) with typical adults has demonstrated differences in neural P180 and N270 responses when the illusory second flash is

perceived versus not perceived, reflecting the neural signatures of multisensory integration (Mishra et al., 2007). The substrates underlying atypical audiovisual integration processes in ASD have not yet been investigated.

Objectives: The present study investigates disruption in neural mechanisms subserving multisensory integration in ASD using the flash-beep illusion. Specifically, this study examines ERP responses to the illusion in children with ASD and typically-developing (TD) controls.

Methods: Participants were 41 children (19 with ASD, 22 with TD) between 10 and 13 years of age (ASD = 11.98 years; TD = 12.05 years, on average). ERPs were recorded with a 128-channel net. Participants were presented with several trial types including a condition with two beeps and one flash and a condition with two flashes and two beeps. Children responded to each trial with the number of flashes they perceived. This allowed for the separation of trials in which the subject did or did not perceive the illusion. Data analysis computed within-group grand-averaged ERPs corresponding to either perceiving or not perceiving the illusion. Results were compared between groups.

Results: Overall, group differences in brain response were found in the N2 and P2 components, reflecting abnormalities in general sensory and illusion-specific multisensory processes in ASD. Across groups, the ERP response over occipital cortex was characterized by a prominent P1 (80-140ms) component that was equivalent whether or not the illusory second flash was perceived. However, across conditions, children with ASD showed a larger than typical N2 (170-230ms) amplitude over visual cortex, suggesting a general difference in sensory processing in ASD. Analysis of ERP response over central and parietal electrodes revealed group differences between illusion and no-illusion conditions, providing neural correlates of multisensory integration. In children with TD, illusion perception was reflected in a double-peaked positive component beginning 180ms post-stimulus and peaking at 230 and 315ms. Children with ASD did not display this double peak; instead, illusion perception elicited heightened amplitude beginning at 180ms at both parietal and central electrodes.

Conclusions: Results help to clarify the neural underpinnings of cross-modal integration in ASD. Specifically, it appears that though both groups are susceptible to a multisensory illusion, the brain mechanisms by which integration occurs differ between ASD and TD. These results contribute to a broader understanding of sensory processing impairments in ASD, having potential to inform refinement of diagnostic assessments and therapeutic interventions.

**117.032 32** An MEG Study of Motor-Related Beta Oscillations during Motor Imitation in Autism. I. Buard*, *University of Colorado-Anschutz Medical Campus School of Medicine*

Background:

As early as 20 months of age, children with autism exhibit a robust deficit in imitating the actions of other people. Diverse explanations for imitative difficulties in ASD have been proposed, including motor and sensory perception control deficits. Indeed, studies have found impairments in many aspects of motor function, including coordination, gait, motor imitation and preparation in both adults and children with autism. Moreover, abnormalities in motor-induced cortical rhythms have been reported in ASD adults while performing motor imitation tasks. To date, however, children with ASD haven't been investigated.

Objectives:

To compare motor-related brain oscillations in control participants to patients with autism during a motor imitation task.

Methods:

Neuromagnetic activity was recorded in 11 children with ASD (including 4 Asperger's syndrome) and 12 typically developing control children, during right hand imitation of finger-lifting movements from an animated right hand projected on a screen facing the subject. Index and little fingers were lifted in response to animations of each finger in random order. Oscillatory changes within the beta frequency band (15-30 Hz) were calculated during and following movement, relative to the baseline activity. Decreased beta power (ERD, event-related desynchronization) was observed prior to and during the movement and imaged using a -500 to 500 msec time window (with time 0 being

the onset of the movement). Following the movement, an increase in beta-band power (PMBR, post-movement beta rebound) was imaged using a 700 to 2000 ms time window. PMBR and ERD of each group were compared at the sensor level in each hemisphere. Eight channels in the vicinity of the motor cortex were selected per hemisphere. Results were averaged per hemisphere and subjected to group statistical analysis using a 2 samples t-test.

Results:

As expected for a right hand movement, we found relevant motor-associated beta oscillations in both hemispheres, contralateral and ispilateral to the movement, during imitation of both fingers. In the left hemisphere (contralateral), ERD was significantly more robust in the autism group compared to the controls for both index ($p=0.01$) and little ($p=0.03$) movements. In contrast, PMBR might have been reduced in ASD subjects, although it did not reach statistical significance, during imitation of index ($p=0.06$) and little ($p=0.07$) lifting movements. In the right hemisphere (ipsilateral), no group difference was found in the beta-band independently of the movement performed.

Conclusions:

These results provide some physiological evidence of distinct brain activity associated with imitation of hand movements in children with autism. ERD reflects movement preparation, and it is possible that the greater ERD in autism was due to increased motor and/or imitation planning difficulty. PMBR is generally associated with motor deactivation or inhibition and has been correlated with GABA concentration within the brain. Our trend towards a reduced PMBR in autism is interesting in light of a recent study showing decreased GABA level in the motor cortex in ASD.

## 118 Cognition: Attention, Learning, Memory

**118.033 33** A Multilevel Meta-Analysis of Executive Function in Individuals with Autism Spectrum Disorders. B. D'Entremont*, E. Boudreau, M. Fulton and D. Voyer, *University of New Brunswick*

**Background:** Individuals with autism spectrum disorder (ASD) are widely reported to have executive function deficits (see Hill, 2004 for review). However, considerable variability has been reported (Hill, 2004; Pennington & Ozonoff (1996). Variables suggested to moderate the influence that ASD might have on executive functions, include executive function domain, whether tasks are human or computer-administered, age, cognitive functioning, verbal ability, and medication. Because these putative moderators are descriptive in the existing literature, firm conclusions cannot be made on how they might moderate the magnitude of deficit. Meta-analysis procedures are well-suited to answer such questions (Borenstein, Hedges, Higgins, & Rothstein, 2009).

**Objectives:** To use meta-analysis to investigate whether executive function domain, administration type (human/computer), age, cognitive function, verbal ability, and medication moderate the effects of ASD on executive functions.

**Methods:** The present meta-analysis examined published and unpublished studies that included a comparison of individuals with ASD and control individuals, matched for mental and chronological age, in tasks that measure executive functioning. The final analysis was based on 134 effect sizes drawn from 71 samples of participants ranging in age from 3 to 41 years. A multilevel approach to meta-analysis was used to handle the presence of non-independent effect sizes and to reflect the hierarchical structure of the data in the overall sample.

**Results:** The overall analysis supported the existence of a significant deficit of medium magnitude in executive functions in individuals with ASD when compared to controls (estimated weighted mean $d= 0.457$). Noteworthy findings were that the effect sizes were largest for planning tasks and smallest for working memory measures. Similarly, effects were reduced when tasks were administered by computer or a combination of media (human and computed), compared to their magnitude when administration was human-based only. Finally, composite measures of executive functions produced smaller effects than pure measures. Interestingly, these findings held across age groups as no significant main effect of that variable, or interactions of age with domain or cognitive level were observed.

**Conclusions:** Results suggest individuals with ASD show deficits in all EF domains examined here. Contrary to suggestions, deficits do not

develop with age; rather deficits were present across ages. Results also suggest that observed executive deficits are not due to the individuals with ASD having lower cognitive or verbal levels. Medications taken by individuals with ASD did not have an effect. Administering tasks by computer may mitigate some of the social-motivational demands associated with face-to-face administration. However, social-motivational demands cannot account solely for the executive function deficits because the effect size for computer administrations was still significant. Finally, effect sizes were smaller when they consisted of composite scores created across conditions, suggesting that conditions within tasks may facilitate or hinder executive function. Further research should be devoted to teasing apart these conditions.

**118.035 35** Assessing the Use of Blink Inhibition As a Measure of an Individual's Level of Engagement with Ongoing Content. C. Ranti*[1], G. J. Ramsay[1], W. Jones[1], A. Klin[1] and S. Shultz[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

Background: One of the guiding goals of autism research is to understand the experience of individuals with Autism Spectrum Disorder (ASD) as they navigate the social world. Our laboratory recently developed a novel method for quantifying a critical aspect of subjective experience: how engaged individuals are with what they're viewing. This measure relies on analysis of dynamic patterns of eye-blinking. Given that blinking results in a brief loss of visual information, viewers unconsciously modulate the precise timing of their eye-blinks. Importantly, viewers are *least likely* to blink when looking at something they perceive to be *most* important or salient. While this measure provides critical insight into what is perceived as engaging by a *group* of viewers, quantifying what an *individual* perceives as engaging presents unique challenges. Individual viewers spend far more time not blinking than blinking – as a result, moments of perceived salience (indexed by statistically significant blink inhibition) are more readily quantified when examining patterns of eye-blinking in a group of viewers. Overcoming these challenges is critical, as individual metrics of perceived stimulus salience have the potential to meet several growing needs in autism research, such as parsing heterogeneity in ASD and the development of diagnostic tools and outcome measures.

Objectives: (1) Assess the feasibility and robustness of individual patterns of eye-blinking as a measure of visual engagement; and (2) quantify deviations in visual social engagement by comparing patterns of eye-blinking in individual children with ASD to TD viewers.

Methods: *Pilot Task:* Eye-tracking data were collected from 20 typical adults. Participants viewed videos that alternated between scenes of water animals and scenes of land animals. Half the participants were instructed to count the number of water animals, and the other half counted land animals. The task was designed so that the two categories of content would be differentially engaging to different groups of viewers. *Natural Viewing Task:* Eye-tracking data were collected from school-age TD children (n=40) and children with ASD (n=49) viewing age-appropriate scenes of social interaction.

Results: As expected, every participant blinked *less* during the scenes that required counting of animals compared with scenes they viewed passively. The difference in blink rate during the task-relevant vs. task-irrelevant scenes was significant, assessed by permutation testing ($p<0.001$). In addition, a linear SVM classifier was trained to assign participants to one of the two experimental groups using the timing of their eye-blinks. The classifier was trained on participants' mean blink rates during each of the water and land scenes and assigned 95% of participants to the correct group. Immediate next steps include using a similar classification approach to compare the timing of eye-blinks made by TD and ASD children during natural viewing of social scenes.

Conclusions: The classifier results demonstrate that it is possible to classify participants by experimental group using individual patterns of eye-blinking. This is an important first step towards demonstrating the feasibility of using eye-blinking as an individual measure of visual engagement, a tool that may provide critical insight into the subjective experience of individuals with ASD.

**118.036 36** Attention to Emotion Expressions in Autism Spectrum Conditions. P. Griffiths*, C. Ashwin and J. Black, *University of Bath*

Background:

Key theories of attentional biases in clinical disorders propose that attention is captured by information relevant to the clinical features of specific disorders. For example, people with spider phobia are often the first people to notice a spider crawling on the wall at a party.People with autism spectrum conditions (ASC) have difficulties in social interactions and understanding the mental and emotional states of others. The social-emotional difficulties seen in ASC are also evident in subclinical people with a high degree of autism traits. To date there has been little research investigatingattentional biases towards information related to the social-emotional difficulties of ASC, including research across the wider spectrum of autism.

Objectives:

The current study investigated attentional biases to emotional expressions in subclinical people with high versus low autism traits and people diagnosed with ASC versus controls. Based on theories of attentional biases in various clinical disorders to information related to their symptoms, we expected people with a high degree of autism traits from the general population and those diagnosed with ASC would show attentional biases towards emotional versus neutral expressions compared to their respective control groups.

Methods:

We recruited 104 participants from the general population and measured their autism traits using the Autism-Spectrum Quotient (AQ). Based on AQ scores we split the sample into two groups: (1) a high autism traits group based on the top quartile of AQ scores, and (2) a low autism traits group based on the bottom quartile of AQ scores. We further recruited 22 people diagnosed with ASC (17 Males) and 22 controls (17 Males). All participants completed a dot probe task where 2 photographs of faces appeared on the display during each trial. One face had an emotional expression and the other had a neutral expression, and the emotional expressions were either negative or positive in valence. The images disappeared after 500ms and participants then responded to target dots appearing in the location where one of the images appeared. Faster RT's to the dots represented enhanced attention towards that picture type.

Results:

Results revealed that subclinical people with a degree of autism traits had faster RT's for dots appearing behind emotional versus neutral expressions, regardless of the valence. Individuals with ASC also showed faster RT's for dots appearing behind emotional versus neutral expressions compared to the control group; however this effect was specific to emotional expressions with a negative valence.

Conclusions:

Results showed that people diagnosed with ASC show attentional biases towards emotional expressions, which is consistent with theories proposing attentional biases related to clinical symptoms. The findings further

revealed that these attentonal biases towards emotional expressions extend to the wider spectrum of autism, with the bias also found in subclinical people with a high degree of autism traits. Results suggest that everyday difficulties understanding the mental states of others enhances the salience of social-emotional information for those with a high degree of autism traits, and that this information captures attention.

**118.038 38** Changes in the Focus of Attention Across Time in Individuals with Autism: The Effect of a Dual-Stream Paradigm. J. L. Ringo*[1], L. N. Jefferies[2], V. Di Lollo[3], J. T. Enns[4], A. Bennett[5] and J. A. Burack[1], (1)*McGill University*, (2)*Murdoch University*, (3)*Simon Fraser University*, (4)*University of British Colombia*, (5)*Lester B. Pearson School Board*

Background: The attentional blink (AB) paradigm has been used to explore the temporal and spatial dynamics of visual attention (Raymond, Shapiro, & Arnell, 1992). In a typical AB paradigm, two target letters are embedded in a rapid stream of digit distracters. Although identification accuracy of the first target is normally very high, identification of the second target is impaired when it appears in close temporal proximity to the first. A notable exception to this occurs when the second target is presented directly after the first target (at the position known as Lag 1). In this case, the AB is much reduced and second-target identification is spared – a phenomenon known as Lag-1 sparing (Potter, Chun, Banks, & Muckenhoupt, 1998). Lag-1 sparing can also occur to targets in different spatial locations (i.e., in dual streams), but only if the second target falls within the focus of attention (Jefferies, Ghorashi, Kawahara, & Di Lollo, 2007).

Objectives: In order to assess the difficulties displayed by persons with ASD in focusing on target stimuli (Ames & Fletcher-Watson, 2010; Burack, 1994), we used a dual-stream AB paradigm to further assess the nature of the narrowing of attention in autism.

Methods: Eleven high-functioning young adults with autism and 18 typically developing (TD) young adults who were matched on chronological age, were tested on a dual-stream AB task in which two target letters were embedded in streams of digit distracters. One stream was presented to the left of a central fixation point, the second stream appeared to the right of fixation. The two targets appeared randomly in either the same stream as one another (same-stream condition) or in opposite streams (different-stream condition). On a third of the trials, the second target appeared immediately after the first (Lag 1); on another third of the trials the targets were separated by a single digit distracter (Lag 3); on the remaining trials, the targets were separated by 8 distracters (Lag 9). Each participant was tested with both an 80-ms and a 133-ms stimulus onset asynchrony (SOA).

Results: The TD participants displayed the expected Lag-1 sparing at the short SOA (80 ms) but not at the long SOA (133 ms), consistent with a focus of attention that is initially broad and that narrows over the course of approximately 50 ms. For those participants with autism, however, no Lag-1 sparing was evident at either SOA.

Conclusions: Previous research has reported that Lag-1 sparing occurs for individuals with autism in a single-stream AB paradigm (Amirault et al., 2009; Rinehart et al., 2010). Our finding, therefore, that Lag-1 sparing does not occur in a dual-stream paradigm is somewhat surprising. We hypothesize that the combination of task difficulty and dynamic changes to focused attention in the dual-stream task, prevented Lag-1 sparing in individuals with autism, but not in TD individuals. Future research will investigate whether an unusually efficient attentional gate underlies the observed differences between TD individuals and those with autism.

**118.039 39** Transitive Inference in Children with Autism Spectrum Disorder and Limited Verbal Ability. C. L. Thomas*, S. B. Gaigg and D. M. Bowler, *City University London*

Background:

Memory functioning in Autism Spectrum Disorder (ASD) follows a characteristic pattern, including good rote memory (Kanner, 1943) and cued recall (Bowler, Matthews & Gardiner (1997). Impairments have been demonstrated in the free recall of semantically related items (Tager-Flusberg, 1991), and the recognition of combinations of features (Bowler, Gardiner & Gaigg, 2008). This suggests a difficulty with *relational binding* - the ability to encode items and events, and the relationships between them, to

allow for adaptive use of the information (Opitz, 2010).

Objectives:

Studies of relational binding have mainly been carried out with verbally able adults with ASD, using verbalisable stimuli (e.g. lists of words. The current study aims to extend these findings to lower-functioning individuals with ASD. A non-verbal, transitive inference paradigm is adapted (Maclean, 2008); (if A > B, and B > C, then A > C). Typical adults tend to use a relational strategy during these tasks (Moses, Villate, and Ryan, 2006), whereas non-human animals tend to use an associative, pair-by-pair strategy (von Fersen et al, 1991), suggesting that language is important in the construction of relational strategies.

Methods:

20 children with ASD and limited verbal ability, and 20 typically developing children matched on non-verbal IQ. Replicating Maclean et al's paradigm, pairs of stimuli are presented in hierarchical order, with participants required to find the "higher-ranked" of the two by touching it onscreen; feedback is given regarding their choice. A test phase is then presented, comprising two trial types: adjacent pairs of stimuli from the training phase, and re-pairings of the stimuli into novel combinations of non-adjacent stimuli (e.g. B-D). Participants must use information from the adjacent training pairs to infer which is the higher-ranked stimulus of each non-adjacent pair, which requires the flexible processing of the relations between pairs. The current study predicts no group differences in the training phase or in the test phase where adjacent stimuli are presented, whereas participants with ASD will be impaired in the non-adjacent pairs, due to the flexible relational binding required to solve those trials.

Results:

Preliminary data show no group differences throughout the training blocks, although a main effect of training block was found, $F(2,8) = 5.03$, $p = .04$, $\eta_p^2 = .56$, indicating a decrease in performance as the blocks become more complex, although performance was > 70% for all participants throughout training. During the test phase no difference in performance was found between the two trial types (adjacent and non-adjacent); there was a significant group difference, $F(1,4) = 10.0$, $p = .03$, $\eta_p^2 = .71$, indicating that the typically-developing participants performed significantly better overall, regardless of trial type.

Conclusions:

Results indicate that, during the test phase, children with ASD and limited verbal ability perform significantly worse, despite having performed above chance during training. This in part confirms the idea that language ability is important in this type of task; the fact that performance in the ASD group was worse overall during the test phase will also be discussed in light of theoretical perspectives on transitive inference.

**118.041 41** Exploring Attentional Strategies for Emotion Recognition in Autism Spectrum Disorders. E. Birmingham*[1], V. Kling[1], N. Roberts[1], D. A. Trevisan[1], J. Tanaka[2] and G. Iarocci[1], (1)*Simon Fraser University*, (2)*University of Victoria*

Background: A key hypothesis in the field of emotion recognition is that children with autism spectrum disorders (ASD) use abnormal attentional strategies to detect emotions in faces, leading to impaired behavioral performance. Eye tracking studies that have tested this possibility, however, have led to conflicting results. Moreover, because eye position can be dissociated from the allocation of attention (Klein & Pontefract, 1994), these previous studies may not have been capturing key information about where children with ASD attend when viewing facial expressions of emotion.

Objectives: We used the Moving Window Technique (MWT) in which the observer explores a blurry face using a mouse-controlled window of high-resolution information (Birmingham et al., *Child Devel* 2012). The MWT confers an advantage over eye tracking by directly revealing the attentional strategies used to decode basic facial emotions.

Methods: Typically developing (TD; N=82) and ASD (N=59) children aged 7-14 years were tested. Within the MWT paradigm, 40 images consisting of four basic expressions (happy, angry, fearful, disgusted) were presented to children in a four-alternative-forced-choice design.

Children had up to 15 seconds to explore each face.

Results:

**Accuracy & RT.** Children with ASD were less accurate and slower than typically developing children at judging emotion expression (accuracy: $F(1,143)=9.46$, $p<.01$; RT: $F(1,143)=10.79$, $p<.01$). Main effects of Emotion revealed that accuracy and RT were best for Happy faces, worst for Angry faces, with intermediate performance for Disgusted and Fearful faces (accuracy: $F(3,429)=46.45$, $p<.001$; RT: $F(3,429)=60.97$, $p<.001$).

**Exploration patterns.** Surprisingly, both groups of children explored the mouth more than any other region, followed by the nose, left eye, right eye, and finally the remainder of the face and the hairline region (main effect of Region: $F(5, 715)=542.63$, $p<.001$). However, exploration patterns differed across emotions, with the eyes explored relatively more, and the mouth relatively less, on angry faces than on disgusted, fearful, and happy faces (Emotion x Region interaction, $F(15, 2145)=23.66$, $p<.001$).

Exploration patterns were remarkably similar in the ASD and TD groups (n.s. Diagnosis x Region interaction); however, they diverged for fearful and angry expressions (significant Diagnosis x Emotion x Region interaction, $F(15, 2145)=1.99$, $p<.05$). Specifically, for angry and fearful expressions, children with ASD tended to explore the mouth more than TD children; no such differences in exploration were found for happy and disgusted expressions.

**Correlations between accuracy and exploration.** Controlling for age, we found that in the ASD group, accuracy for detecting fear and anger was positively correlated with exploration of the left eye (angry: $r = 0.39$, $p<.01$; fear: $r = 0.33$, $p<.01$) and the right eye (angry: $r = 0.26$, $p<.05$ ; fear: $r = 0.33$, $p < .01$), and was negatively correlated with exploration of the mouth (angry: $r = -0.26$, $p<.05$; fear: $r = -0.37$, $p<.01$). No correlations between accuracy and exploration time were found for the typically developing children, or for happy and disgusted faces regardless of diagnosis.

Conclusions: Despite largely similar attentional strategies for recognizing emotions, we find subtle differences in ASD that contribute to their reduced behavioral performance.

**118.042 42** Verbal Memory and ADHD Symptoms in Higher Functioning School-Aged Students with ASD. T. Oswald*[1], N. S. McIntyre[1], S. Novotny[1], L. E. Swain-Lerro[1], J. S. Beck[1], M. Montanez[1], M. Solomon[2] and P. C. Mundy[1], (1)*UC Davis*, (2)*MIND Institute*

Background: Studies of memory in higher functioning children with ASD (HFASD) have yielded inconsistent evidence of impairment (Luna et al. 2007; Ozonoff et al. 2009). In addition, most studies have focused on spatial memory rather than verbal memory, and many have not controlled for possible confounds of diagnostic group differences in IQ or the presence of ADHD symptoms. The latter is especially important because working memory impairments are associated with ADHD (Kofler et al. 2010; Sinzig et al. 2009) and research indicates that ADHD is comorbid with ASD at a rate of 50% or higher (Goldstein & Schwebach 2004).

Objectives: To examine whether there are verbal memory deficits specific to children with HFASD, and whether the nature of these deficits are related to individual differences in comorbid ADHD symptoms in these children

Methods: The study consisted of 144 participants (109 male; 35 female) ranging in age from 7.9 to 16.1 years ($M = 11.40$, $SD = 2.19$): 31 with HFASD, 43 HFASD + ADHD Combined, 25 with ADHD, and 40 TD. ASD diagnosis was assessed with the ADOS-G, Connors-3 Parent Report total t-scores > 70 were used to assign children to the ADHD subgroups. The TD group had a significantly higher full-scale IQ (114.59) than the HFASD (101.91), Combined (99.16), and ADHD (99.15) groups. Verbal memory was assessed with the WRAML-2 "Story Memory" recall subtest and the "Verbal Working Memory" (WM) subtest.

Results: MANCOVA for Story Memory and Verbal WM with IQ as a covariate revealed a significant effect for Diagnostic Group, Wilks' $\Lambda = .75$, $F(6, 266) = 6.81$, $p < .001$, $h^2 = 0.13$. Univariate tests revealed Diagnostic Group effects for both variables: Story Memory ($F(3, 134) = 7.74$, $p < 0.001$, $\eta 2 = .15$) and Verbal WM subtests, ($F(3, 134) = 9.60$, $p < 0.001$, $\eta 2 = .18$). Follow-up tests for Story Memory revealed that the HFASD

group and HFASD-ADHD combined group did not differ from each other but scored significantly lower than the TD group, and the combined group also scored significantly lower than the ADHD group (Bonferroni, *p*s < .001). All three diagnostic groups scored lower than the TD group on Verbal WM (Bonferroni, *ps*< .01).

Conclusions: Our findings indicate that the HFASD group, irrespective of ADHD symptoms, was impaired on verbal WM relative to TD children. In addition, the HFASD group and HFASD-ADHD combined group did not differ on story memory but had significantly poorer story recall than the TD group, and the HFASD-ADHD Combined group was distinguished from the ADHD group by impairments in story recall. The Story Memory task may reflect executive control in Verbal WM (Baddeley & Wison, 2002). If so, the data suggest that children with HFASD, especially those who have elevated ADHD symptoms, may be particularly vulnerable to impairments in this component of Verbal WM. Other observations in our research group suggest HFASD verbal memory impairment is not affected by anxiety symptoms, but does negatively impact academic communication development (Swain et al. 2014; Zajic et al. 2014).

**118.044 44** Dimensionality of Gaze Patterns Towards Faces and Objects in Toddlers with ASD. Q. Wang*[1], K. Chawarska[1], S. W. Zucker[2], B. Scassellati[2] and F. Shic[1], (1)*Yale University School of Medicine*, (2)*Yale University*

**Background:** Eye-tracking is a prominent tool in psychological and cognitive research. However, the analysis of eye-tracking data is confounded by choices in how fixations should be defined, i.e. how densely packed points must be in order to be considered a fixation. Our previous work (Shic, Scassellati, & Chawarska, 2008), has shown that by manipulating fixation parameters, the fixation statistics between ASD and TD toddlers can reversed. There exists evidence that scale-free fractal structure may derive from gaze patterns of viewing naturalistic stimuli.

**Objectives:** (1) To explore the nature of toddlers' scanning patterns during complex scene viewing, independent of fixation parameters. (2) To apply this technique to examine scale-free gaze behaviors in toddlers with Autism Spectrum Disorders (ASD) and typical development (TD) when looking at faces and blocks.

**Methods:** We presented 6 trials (10s/trial) with pictures of faces and 6 trials with block designs to TD toddlers (*n* = 12, Mean age=23.8(±2.8) months) and toddlers with ASD (*n*=10, Mean age=22.7 (±3.7) months). We examined the log of the number of fixations (n) as a function of the log of box size (s) ranging from .1 deg. to 10 deg. This is a greedy box-counting algorithm for fractal dimensionality, equivalent to an adaptation of fixation identification algorithms at multiple distance scales.

**Results:** The smallest *R*-squared in our linear regression is $R^2$=.944, with an average of $R^2$=.992, suggesting that the scanning patterns were strongly self-similar and that measures of gaze pattern fractal dimensionality through box counting is robust. A mixed linear model on the box count dimensionality of our eye tracking data revealed a main effect of stimulus class (p<.01) with a higher dimensionality for blocks than faces. An interaction was found for group and stimulus class (p<.05) driven by a lower dimensionality for faces than blocks in TD toddlers, but no such effect for toddlers with ASD. There was a trend for toddlers with ASD to exhibit higher dimensionalities for scanning faces (p=.08). Our results are consistent with lower dimensionalities being associated with more directed patterns of scanning.

**Conclusions:** Our use of fractal dimensionality may offer a route to more robust, more informative, and less biased approaches towards eye-tracking analysis. Consistent with previous experiments, our study, which reports on box counting fractal dimensionality, suggests that TD toddlers use different basic attentional strategies to process faces and blocks, whereas toddlers with ASD may be employing similar distributional strategies for both stimuli classes.

**118.045 45** Impaired Voluntary Imitation of Biological Motion in Autism Spectrum Conditions. S. J. Hayes*[1], M. Andrew[1], D. Elliott[2], E. Gowen[3] and S. J. Bennett[1], (1)*Liverpool John Moores University*, (2)*McMaster University*, (3)*University of Manchester*

**Background:** Imitation is intricately linked to developing social relationships and motor learning. These interpersonal contexts require the appropriate imitation of biological motion, which is suggested to be impaired in autism spectrum conditions (*autism*) due to processes underpinning social modulation and motor control. These

suggestions were based on examining biological motion during automatic imitation, with human models, and manipulating movement speed. Here, we examined voluntary imitation using a novel methodology that displayed three models with the same movement time, but different biological motion kinematics. To control for modulatory effects of social context, we used a non-human agent model (single white dot).

**Objectives:** The objectives were to: (1) examine imitation of biological motion kinematics; (2) examine underlying motor control processes learned from acquiring a 3-segment motor sequence timing task (*motor task*).

**Methods:** Twelve adults with *autism,* diagnosed by a clinical assessment and ADOS, plus twelve adults (*control*) participated in the study, which was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee. In Phase 1, each participant imitated, using a stylus on a graphics tablet, different models displaying distinct velocity profiles: *unnatural velocity* (biological); *natural velocity* (biological); *constant velocity* (non-biological). The movement time of each model was 1700 ms. In Phase 2, each participant physically practised, with feedback, a motor task that had a movement time goal of 1700 ms.

**Results:** Compared to the *control* group, data from Phase 1 indicated that participants with *autism* imitated movement time over trials to become significantly closer to the model time ($p$<.05). The kinematic data showed no difference between the participants with *autism* and *control* participants when imitating *natural* and *constant velocities* ($ps$>.05). However, the *control* participants imitated *unnatural velocity* more accurately than the participants with *autism* ($ps$<.05). In Phase 2, the performance data indicated the *autism* and *control* groups became significantly more accurate and consistent over trials ($ps$<.05). The kinematic data indicated that over trials the participants with autism did not increase peak limb acceleration in the ballistic phase of the movement as per the *control* group ($p$<.05). A correlational analysis indicated a relationship between imitation accuracy of *unnatural velocity* and peak acceleration for the *control* group ($p$=.058), but not the *autism* group ($p$>.05).

**Conclusions:** Using non-human agent models, we observed that imitation of biological motion kinematics is impaired in *autism*, but that imitation of the temporal properties of the model became more accurate over trials. These findings suggest the deficit in imitating biological motion might be related to persons with autism orientating attentional focus to the temporal goal at the expense of kinematics. Although the general sensorimotor processes associated with learning a motor task are functional in *autism,* a difference was observed in planning and executing the ballistic phase of the movement. When correlated with imitation accuracy, no relationship was observed between motor control and imitation of biological motion in participants with *autism*. These findings suggest impairments in imitating biological motion in autism spectrum conditions is most likely related to focusing attention to the temporal goal.

**118.046 46** Is Cognitive Variability a Viable Candidate Endophenotype for Autism? Results from a Broader Autism Phenotype (BAP) Study. A. L. Hurley*[1], D. H. Skuse[2], C. O'Mahony[3], P. Burgess[3] and W. Mandy[2], (1)*Great Ormond Street Hospital*, (2)*UCL Institute of Child Health*, (3)*UCL Institute of Cognitive Neuroscience*

Background:

Conflicting accounts of the cognitive profile of autism have long presented a challenge for theorists seeking to explain the neuropsychological processes underlying this complex disorder. Although cognitive impairments among individuals with ASD have been widely reported, as well as superior performance on some measures, there are many inconsistencies in the literature (see Hill, 2004, and Happe & Frith, 2006). It has recently been suggested that cognitive variability, resulting from disruption to the normal processes of brain specialisation (Gilbert, 2008), may in fact be a core feature of ASD. Using multiple-case series analyses, a number of recent studies have reported a highly significant pattern of within-participant cognitive variability among individuals with autism, with evidence of both sub- and supra-normal performance (Towgood, Meuwese, Gilbert, Turner, & Burgess, 2009) particularly on measures of rostral pre-frontal cortex (rPFC) functioning (O' Mahony, 2009).

Objectives:

This study aimed to evaluate whether cognitive variability represents a viable candidate endophenotype for autism through investigation of cognitive profile of the broader autism phenotype (BAP). Specifically, the study sought to investigate whether fathers of children with ASD would show greater variability in their cognitive profile, including higher incidence of a pattern of both impaired and superior performance, relative to controls. The study also examined whether cognitive variability among fathers of children with ASD would correlate with self-rated social, communication and behavioural difficulties. Finally, the study investigated whether fathers of children with ASD would show greater impairments on measures of rPFC functioning than controls.

Methods:

The performance of twenty-four fathers of children with ASD and twenty control fathers was compared using a test battery that predominantly assessed rPFC functioning. Measures of IQ, social cognition and information processing were also administered. Group-difference and multiple-case series analyses were used to explore patterns of performance between groups and within each individual's cognitive profile.

Results:

Multiple-case series analysis indicated that fathers of children with autism did not display significant cognitive variability relative to controls and there was no evidence of greater incidence of a pattern of both impaired and superior performance. Analysis at the group level found no significant difference between the groups in relation to measures of rPFC functioning. A significant group difference emerged in relation to Theory of mind, but this did not survive Bonferroni correction.

Conclusions:

The results suggest that cognitive variability is not a feature of the broader autism phenotype and that it is unlikely to represent a candidate endophenotype for ASD. While individuals with ASD may show high levels of variability in their cognitive profiles, rather than being a core feature of ASD, it may reflect a secondary feature of the disorder.

**118.047 47** Neurocognitive Strategies Supporting Behavioral Response Inhibition in ASD. L. M. Schmitt*[1], M. W. Mosconi[2], M. E. Ragozzino[3], E. H. Cook[3] and J. A. Sweeney[2], (1)*Center for Autism and Development Disabilities, UT Southwestern Medical Center*, (2)*Center for Autism and Developmental Disabilities, UT Southwestern Medical Center*, (3)*University of Illinois at Chicago*

Background: Executive dysfunctions, including deficits in behavioral response inhibition, have been repeatedly documented in ASD. A reduced ability to voluntarily inhibit prepotent eye movements has been shown to be related to the severity of patients' repetitive behaviors. We recently demonstrated that the ability to inhibit an unwanted or inappropriate behavior is enhanced by strategically delaying the onset of that behavior. Both behavioral response inhibition and these strategic biases in response timing are supported by frontostriatal brain systems. Assessments of behavioral response inhibition and strategic biases in response timing are therefore important for characterizing patterns of frontostriatal dysfunctions in ASD and the neurocognitive bases of repetitive behaviors.

Objectives: To characterize behavioral response inhibition deficits and underlying neurocognitive strategies in individuals with ASD using oculomotor and manual stop signal tasks.

Methods: Sixty-nine individuals with ASD and 56 healthy controls matched on age (range 6-38 years), gender, and nonverbal IQ were administered manual motor and oculomotor stop-signal tasks (SST). Participants were instructed to either press a button (manual version) or make a saccade (oculomotor version) when a peripheral target appeared ('GO' trials), or inhibit these responses when a central stop signal appeared at varying times following the appearance of the peripheral cue ('STOP' trials). GO and STOP trials were interleaved. Oculomotor and manual motor baseline reaction time (RT) tasks consisting only GO trials were administered to assess adaptive RT slowing during the SST GO trials. The Autism Diagnostic Interview-Revised (ADI-R) was used to assess social-communication deficits and repetitive behaviors.

Results: Subjects showed increased RTs for both oculomotor and manual motor SSTs relative to baseline, indicating that they strategically delayed their responses when STOP trials were interleaved with GO trials. Greater RT slowing during the

SSTs was associated with increased accuracy on STOP trials. During both SSTs, participants with ASD made more STOP trial commission errors than healthy controls, and they did not slow their reaction times as much as controls. Response inhibition performance was similar across tasks in healthy controls, but performances on the SSTs were not related in subjects with ASD. Increased STOP trial error rates and reduced RT slowing relative to baseline during the manual SST each were related to higher-order repetitive behaviors in ASD.

Conclusions: Individuals with ASD show deficits inhibiting prepotent behavioral responses that involve failures to strategically delay their responses in the context of uncertainty. Importantly, both increased error rates and reduced strategic slowing each appear to contribute to higher-order repetitive behaviors in ASD, including compulsive and ritualistic behaviors and circumscribed interests. Behavioral response inhibition is supported by discrete frontostriatal circuits, including medial prefrontal cortices that are involved in strategically delaying response onset during conditions in which caution and speed must be dynamically balanced. Thus, our current findings suggest that pharmacological treatments targeting frontostriatal circuits, and cognitively mediated therapies targeting top down behavioral control, each may be useful for reducing higher-order repetitive behaviors in ASD.

**118.048 48** Orienting Response, Viewing Preference, and Exploration Patterns in Young Children with ASD. C. McCormick*[1], G. S. S. Young[2], J. Bernstein[2] and S. J. Rogers[2], (1)*University of California, Davis*, (2)*UC Davis MIND Institute*

**Background:** Some evidence suggests that when children with typical development (TD) view pictures of faces they exhibit an orienting response and preference for faces over other stimuli (Gliga et al., 2009). Findings in Autism Spectrum Disorders (ASD) vary with evidence for a diminished preference for faces (Chawarska et al., 2010), preference for objects of high interest (Sasson et al., 2011), or no difference in attention (Fischer et al., 2013) compared to TD peers. Causes for differing results could be complexity or saliency of images, age, developmental level, or amount of intervention received.

**Objectives:** To investigate orienting response, preference, and exploration patterns of young children with ASD while viewing complex visual arrays of faces and objects.

**Methods:** To date, 14 children with ASD (10 male) with mean age 28.86 (SD = 5.48) and 15 children with TD (10 male) with mean age 23.20 (SD = 5.19) have completed the protocol. Children in the ASD group were either receiving less than 10 hours a week of intervention or had not been enrolled in intensive intervention for longer than two months. Participants were presented with 10 different circular visual arrays. Each array contained 3 smiling adult faces varying in gender and ethnicity (Caucasian, African American, East Asian, Indian, and Hispanic) and 3 novel, colorful toys. Each array was not displayed unless the child was fixated at the center of the screen and was then presented for six seconds. We measured orienting response (percent of first fixations to a face), preference (percent of looking time to faces), and exploration (number of images viewed).

**Results:** Within group t-tests revealed that first look to face versus object images in both the ASD and TD groups was at chance (ASD $t(13) = .20$, $p = .85$; TD $t(14) = .88$, $p = .39$). There was no group difference in percent of first look to a face ($t(27) = .66$, $p = .51$). There was also no group difference in percent of looking time to faces ($t(27) = .89$, $p = .38$). Children in the ASD group explored more object images than the TD group ($t(27)2.58$, $p = .02$), but there was no group difference in exploration of face images ($t(27)$ .46, $p = .65$).

**Conclusions:** In an array of complex images of objects and faces, children with ASD and TD showed no preference for either type of image, either through an orienting response or overall looking time. Children with ASD demonstrated more exploration behavior of object images. Evidence in older children suggests that children with ASD engage in more visual exploration when viewing highly interesting objects (Sasson et al., 2011). High exploration in the ASD group may be influenced by the novelty or saliency of the objects.

**118.049 49** Patterns of Impairment Among School Aged Children with ASD As Measured with a Computerized Executive Function Battery and Parent Report. C. Sonners*, N. Nayudu, G. Greco and S. Faja, *University of Washington*

Background: Among individuals with autism spectrum disorder (ASD), difficulties with executive function are observed, though the social demands of traditional laboratory tasks may contribute to differences in performance (Kenworthy et al., 2008). Flexibility and generativity impairments have been well documented, but investigations of working memory and inhibition have been mixed. The current project employed a computerized battery of behavioral tasks as well as parent report of executive dysfunction. The focus of the battery was examination of inhibition and verbal working memory.

Objectives: To explore whether inhibition and working memory performance differed between children with ASD and typically developing comparison children. To investigate parent report of inhibition and working memory between groups. To evaluate the effect of age on performance in order to determine whether group differences may represent delays in development among young children with ASD.

Methods: Data collection is ongoing with data currently available for 16 children with ASD and 17 children with typical development (TD). Participants are 7 to 11 year-olds with full scale IQ of 80 or above. Inhibition was measured using a computerized version of the Stroop task and the Change task, which included a Go-Nogo block and a block of shifting from the dominant to a subdominant response (i.e. Change block). Working memory was measured using a computerized version of the Children's Memory Scale Numbers subtest. Parent report of inhibition and working memory were also collected via the Behavioral Rating Inventory of Executive Function (BRIEF). Full scale IQ was covaried in all group comparisons.

Results: Preliminary results indicate group differences on percent accuracy between the neutral and incongruent conditions of the Stroop task, $F(1, 21) = 11.2$, $p = .003$. During the Change task, groups differed in accuracy during the Go-Nogo block, $F(1, 30) = 4.6$, $p = .04$, but did not significantly differ in the Change block. In terms of working memory, groups did not differ in their backward digit span performance. By parent report, children with ASD had more executive function difficulties overall, $F(1, 24) = 31.7$, $p < .001$, as well as reduced inhibition, $F(1, 24) = 11.2$, $p = .003$, and working memory, $F(1, 24) = 11.1$, $p = .003$. Among children with ASD, age was related to reaction time on the Stroop, $r(11) = .62$, $p = .04$, accuracy during the Go-Nogo block, $r(16) = .76$, $p = .001$, and the Change block, $r(16) = .61$, $p = .01$, of the Change task. Age did not relate with verbal working memory during the Digit Span.

Conclusions: Preliminary results suggest that children with ASD differed from those with TD on behavioral measures of inhibition in the face of conflict, but not verbal working memory. Parent report of inhibition, working memory, and overall executive function suggests more widespread difficulties among children with ASD relative to the comparison group. Interestingly, age corresponded with behavioral performance on measures of inhibition among children with ASD, providing support for a delay in this domain among young school aged children without significant cognitive impairment.

**118.050 50** Profiles of Executive Function in Austim Spectrum Disorders and Attention Deficit/Hyperactivity Disorder. C. Mills*[1], M. Berl[2], L. Kenealy[1], K. Dudley[1] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*Chidlren's National Medical Center*

Background: Executive function (EF) impairments are common in many developmental disorders. However, questions remain as to whether patterns or profiles within executive function subdomains distinguish one disorder from another. For example attention deficit hyperactive disorder (ADHD) has been associated with particular problems with inhibition and working memory, while autism spectrum disorder (ASD) has been linked to problems with flexibility. Approximately half of children diagnosed with ASD also meet diagnostic criteria or exhibit clinically significant symptoms of ADHD-Combined Type or ADHD-Inattentive Type.

Objectives: To compare the profiles of EF subdomains in children diagnosed with ADHD-Combined Type (ADHD-C); ADHD-Inattentive Type (ADHD-I); ASD, ASD with comorbid ADHD-C (ASD+ADHD-C), and ASD with comorbid ADHD-Inattentive Type (ASD+ADHD-I).

Methods: Executive functioning was assessed in a sample of 224 children (166 males, 58 females, age range 5-18 years; mean = 9.8, SD = 2.7) at Children's National Medical Center, as part of a

neuropsychological evaluation or research protocol, with parent ratings of the Behavior Rating Inventory of Executive Function (BRIEF). The sample included the following clinical diagnostic groups: ASD (n=76), ASD+ADHD-C (n=23), ASD+ADHD-I (n=25), ADHD-C (n=73) and ADHD-I (n=27). The clinical groups were matched for gender, age and IQ. A repeated measures ANOVA was conducted to evaluate main and interacting effects between diagnostic category and BRIEF subscale (Inhibition, Shift, Emotional Control, Initiation, Working Memory, Planning/Organization, Organization of materials, and Monitor).

Results: Results revealed a significant main effect of BRIEF subscale ($F(7, 1498) = 17.930$, $p < .001$), partial eta squared = .077). Post hoc analysis revealed that among all the diagnostic groups combined, Working Memory (M t-score=67.38) and Shift (M t-score=66.11) showed the greatest impairment, whereas Organization of materials (M=59.41) was least affected. The main effect of diagnostic group was also significant ($F(4,214) = 14.12$, $p=.000$, partial eta squared =. 209). Post hoc analysis revealed that the ASD and ADHD-I groups where less impaired overall on the BRIEF than the other groups. Across the BRIEF subscales, comorbid ASD+ADHD-C demonstrated the most executive dysfunction, followed by ASD+ADHD-I, particularly on the Shift, Working Memory, and Plan/Organize subscales. A significant interaction effect between the diagnostic groups and the BRIEF subscales was also found, ($F(28, = 6.089$, $p=.000$, partial eta squared =.102), with unique profiles associates with specific diagnostic groups.

Conclusions: These findings suggest differences among diagnostic groups in both the severity of parent reported EF problems overall and in specific subdomain profiles, which supports recent changes in the Diagnostic and Statistical Manual-5 allowing the diagnosis of ADHD with ASD and also indicates a need for targeted treatment methods with in the EF domain.

**118.051 51** Recognising the Same Face in Different Contexts: Testing within-Person Face Recognition in Autism. L. E. Neil*[1], G. Cappagli[1], T. Karaminis[1], R. Jenkins[2] and E. Pellicano[1], (1)*Centre for Research in Autism & Education, Institute of Education*, (2)*University of York*

Background:

Difficulties recognising faces are well established in autism. Yet research into face recognition has focused exclusively on the ability to tell people apart, rather than on recognising the same face in different contexts. One recent study highlighted the scale of 'within-person variability' by demonstrating that typical adults frequently perceive differing images of the same person as different people. Effective within-person face recognition relies on using within-person variability to build stable representations of a person's appearance. According to current theoretical accounts of autistic perception, people with autism might be less likely to make use of this variability in the generation of robust internal working models of the world. We therefore expected that children with autism would have problems extracting the variability among different images of the same face, making identity judgments about the same person across contexts difficult.

Objectives:

To extend research on within-person variability in face recognition to autism, by comparing autistic children and typically developing children on their ability to recognise the same identity across different images.

Methods:

Twenty-one children with autism (M age=10.62; SD=2.80) and 21 typical children (M age=10.51; SD=2.43), of similar age and intellectual ability, participated. Following a previous study, children were given 40 grayscale photographs of two distinct male identities (20 of each face; taken at different ages, from different angles and in different lighting conditions) and asked to sort them by identity within a ten-minute time limit. Importantly, children were never told how many identities to expect; they were simply to inspect the images and group them into as many identities as they perceived. We recorded the number of identities children produced (out of 40) and the number of misidentification errors per perceived identity. We predicted that children with autism would find it difficult to map diverse photos onto the same face, resulting in solutions that contained more identities than were actually presented and greater numbers of misidentification errors.

Results:

Just like typical adults, children in both groups mistook images of the same person as images of different people, subdividing each individual into many perceived identities. While children with autism reported a similar number of identities (median=17, range=2 – 39) to typical children (median=16; range=3 – 33), they nevertheless made significantly more misidentification errors than typical children, incorrectly placing images of different identities in a single pile. Further analysis of these errors showed that, out of 400 possible mismatches between 20 images of 2 different identities, children with autism made a total of 363 mismatches compared to only 88 for typical children.

Conclusions:

Within-person variability poses a considerable challenge to face recognition, yet has so far been neglected by autism researchers. Results suggest that children with autism may have greater difficulties than typically developing children in recognising the same facial identity shown across contexts – just as they do in telling different faces apart. We suggest that these difficulties arise as a result of problems extracting the perceptual commonalities from different images of the same person and building stable representations of facial identity.

**118.052 52** Relations Between Basic Indices of Attention to Social Events and Language in Children with Autism Spectrum Disorders and Typically Developing Children. J. T. Todd*, J. F. Saunders, V. Bein, K. C. Soska and L. E. Bahrick, *Florida International University*

Background: Basic attention and intersensory processing skills are foundations for typical social-communicative development (Bahrick & Lickliter, 2012) and children with autism spectrum disorders (ASD) show impairments in these skills (Bebko etal., 2006; Bahrick & Todd, 2012). The Multisensory Attention Assessment Protocol (MAAP; Bahrick etal., 2011) assesses four basic indices of attention (disengagement, orienting, maintenance, intersensory processing) to audiovisual events. It distinguishes between typically developing (TD) children and children with ASD in attention maintenance and disengagement to look to social events and can identify a subgroup of ASDs (ASD-FTD; those who fail to disengage from a competing central stimulus) who show enhanced attention deficits and symptom severity (Bahrick etal., 2012).

Objectives: We investigated relations between basic attention indices (MAAP) and language functioning (Mullen Scales of Early Learning, 1995) in ASD and TD children. Given that intersensory processing and attention to faces are critical for learning language (Bahrick & Lickliter, 2012; Bahrick & Todd, 2012) we expected that indices of attention to social events would predict concurrent language functioning in TD and ASD children. Further, we predicted that ASD-FTD children would show more impaired language functioning than ASDs and TDs who show no failures to disengage.

Methods: Children with ASD (*N*=21; *M*=4.23 years, *SD*=.86), who passed ADOS cutoffs, and TD children (*N*=21; *M*=2.47, *SD*=.50), matched on Mullen nonverbal adjusted age (ASD: *M*=2.61, *SD*=1.29; TD: *M*=2.98, *SD*=.85) participated. In the MAAP, trials of a 3s central visual event were immediately followed by two side-by-side peripheral events (10s), one moving in synchrony with its natural soundtrack. Peripheral events were either social (two women speaking) or nonsocial (two objects striking a surface). Disengagement (latency to shift to peripheral event with the competing central event on), orienting (latency to shift to peripheral event with the central event off), intersensory processing (proportion of looking to sound-synchronous event), and attention maintenance (proportion of trial looking to peripheral events) were calculated.

Results: For the entire sample together (*N*=42), for social (but not nonsocial) events, faster latencies to disengage and orient, and higher intersensory processing and attention maintenance were associated with better Mullen Receptive and Expressive Language raw scores (*r'*s >.30, *p'*s<.05). For TDs, attention maintenance and intersensory processing of social events predicted Expressive Language. For ASDs, attention maintenance and latency to disengage for social events predicted Expressive Language. Further, the ASD-FTD subgroup showed lower Receptive and Expressive Language than ASDs and TDs who showed no failures to disengage (*p*'s<.004).

Conclusions: Basic attention and intersensory processing of social, but not nonsocial, events assessed by the MAAP predicted concurrent Receptive and Expressive language for TD and ASD children. Further, a subgroup of children with ASD who failed to disengage to peripheral events and showed the greatest attention and intersensory processing impairments, showed more severe language impairments compared to TD and other ASD children. Findings demonstrate performance on the MAAP is predictive of social-communicative functioning, highlighting links between social attention and language. Further, this simple method can identify a subgroup of individuals with ASD who are most in need of intervention.

**118.053 53** Spatial and Temporal Effects on Visual Filtering in Autism Spectrum Disorder. J. Stewart*[1], T. Dawkins[1], D. A. Brodeur[2] and J. A. Burack[1], (1)*McGill University*, (2)*Acadia University*

Background:

The ability to filter irrelevant visual stimuli in order to attend to meaningful sources of information is crucial to all aspects of adaptive functioning, as real-life environments involve innumerable and consistently moving and changing stimuli. Among persons with autism spectrum disorder (ASD), visual filtering efficiency has been portrayed in two apparently conflicting ways – increased distractibility (e.g., Burack, 1994) and overfocused attention (Mann & Walker, 2003). According to the increased distractibility hypothesis, persons with ASD are particularly susceptible to distraction by stimuli that are so visually peripheral that they do not affect the processing of typically developing persons, whereas according to the overfocused hypothesis persons with ASD process information within a restricted range regardless of its importance.

Objectives:

The aim of the study was to investigate the effect of temporal and distance manipulations of distracters on target identification among children with ASD. The timing of target and flanker onsets was manipulated to determine whether asynchronous onset of the flankers and target facilitated or disrupted target identification, while the proximity of the flankers to the target was varied to assess the participants' ability to narrow and broaden the focus of attention.

Methods:

The participants included school-aged children with ASD (n= 13) and TD children (n= 13) matched on mental age (mean MA = 8.6 years; $F(1,24) = .008$, $p > .05$). A modified version of the flanker paradigm (Eriksen & Eriksen, 1974) was used, in which participants responded to a 'target' stimulus presented at the centre of a computer screen with distracting 'flanker' stimuli presented to the left and right along the same horizontal plane that varied in shape (similar or dissimilar to target), distance from targets (1.16°, 3.46°, or 6.89° of visual angle), and in temporal onset relative to target onset (simultaneous, or 150ms, 300ms, or 450ms after target).

Results:

Both groups of children displayed faster RTs when flankers were similar to targets than when they were dissimilar. The children with ASD also displayed faster RTs when the flankers and target were presented simultaneously than with onset asynchrony of 150ms ($p = .002$), 300ms ($p = .000$), and 450ms ($p = .001$). Unlike the TD children who had faster RTs when flankers were farther from the targets than when flankers were at an intermediate ($p = .000$) or closer ($p = .000$) distances, the participants with ASD showed similar performance regardless of the distance of the distracters from the target.

Conclusions:

The findings related to both spatial and temporal distracter manipulations support the notion of increased distractibility among persons with ASD, but are inconsistent with the overfocused hypothesis.

**118.054 54** Spatial and Temporal Modulation of Visual-Tactile Crossmodal Interactions in Adults with Autism. D. Poole*, E. Gowen, P. A. Warren and E. Poliakoff, *University of Manchester*

Background:

The sensory issues that affect many people with autism spectrum conditions (ASC) may be explained by abnormalities in how information is combined from the separate sensory modalities when creating a unified perception of the environment (Iarroci and McDonald, 2006). Typically, the processing of crossmodal information is spatially and temporally bound:

information is more likely to interact if it occurs in the same place and at the same time (Stein and Standford, 2008). However, children with autism have previously been shown to exhibit audio-visual interactions over a range of time double the length of neurotypical (NT) children (Foss-Feig et al,2010; Kwakye et al 2011).

Objectives:

The aims of the current study were to:

1. Provide novel insight into visual-tactile interactions in ASC using low-level stimuli, free from social and semantic information.
2. Explore the spatial modulation of crossmodal interactions in ASC.
3. Replicate previous findings of crossmodal interactions over extended temporal asynchronies in ASC.

It was expected that this would provide a more detailed picture of crossmodal interactions in ASC.

Methods:

Participants were 13 adults with ASC and 13 NT controls matched for age, IQ, handedness and gender. Participants completed an adapted version of the crossmodal congruency task (Spence, 2001). The task involves making speeded discriminations between single or double tactile pulses while presented with distracting visual flashes. Distractors were either congruent (e.g. one pulse- one flash), or incongruent (one pulse- two flashes). A baseline condition was also included in which only tactile information was presented. Paired sample t-tests were used to compare error rates between the baseline condition and those including visual distractors. The spatial and temporal modulation of crossmodal effects were investigated in two separate experiments. In the spatial version of the task, distractors were presented 0cm, 21cm and 42cm from the hand in ipsilateral positions, and 42cm from the hand in a contralateral position. In the temporal version of the task, distractors were presented near simultaneously (30ms before) or 100ms, 200ms and 400ms after the tactile pulse.

Results:

For the spatial version of the task, NT participants only produced an error rate significantly larger than the baseline condition for incongruent distractors presented 0cm from the hand. ASC participants exhibited this effect in both the 0cm and 21cm conditions.

Temporal version of the task: After correcting for pairwise comparisons, NT participants did not produce a significant effect at any SOA. Contrary to previous research, participants with ASC only exhibited crossmodal effects in the near simultaneous -30ms condition.

Conclusions:

This is the first work to suggest that crossmodal interactions in ASC occur over greater distances in space than in NT controls. However, the finding of the typical pattern of temporal modulation in adults with ASC contradicts previous findings in the audio-visual modality in children. This suggests that there may be a delay in the development of the temporal modulation of crossmodal information processing in ASC.

**118.055 55** Personality and Perceptual Features of the Broad Autism Phenotype: Eye Gaze during Narration of "Frog, Where Are You?". M. A. Lee*[1], J. Hornickel[1], B. Thomas[1], D. Hamburger[1], P. C. Gordon[2] and M. C. Losh[1], (1)*Northwestern University*, (2)*University of North Carolina-Chapel Hill*

Background:

Converging evidence suggests that subtle social and communication differences are one of the defining features of a larger constellation of subclinical traits indicative of genetic liability in ASD, termed the Broad Autism Phenotype (BAP). Exploring the cognitive mechanisms underlying these features of the BAP is crucial for understanding the development of social deficits in ASD as well as the identification of candidate endophenotypes, or heritable, subclinical traits with more straightforward ties to underlying biology than full clinical syndromes. Individuals with ASD demonstrate atypical visual processing patterns that have been linked to severity of social deficits. Recent research demonstrating that unaffected parents and siblings of individuals with ASD tend to show patterns of visual processing similar to their affected family members when viewing faces and brief videos of non-social stimuli suggests that allocation of visual attention may also underlie these features

in the BAP (Adolphs, Spezio, Parlier & Piven, 2008; Groen et al., 2012; Dalton, Nacewicz, Alexander & Davidson, 2007). However, to our knowledge research has yet to explore perceptual processes *during* communicative acts. Such research is needed to characterize how perceptual strategies ultimately guide the ways in which individuals navigate their social world, and, importantly, how these patterns may contribute to subclinical social differences observed in the BAP.

Objectives:

Using a unique narrative elicitation task, we sought to define patterns of visual gaze in parents of individuals of ASD when actively interpreting social stimuli, and to explore how these patterns related to features characteristic of the BAP.

Methods:

Using TobiiX60 software, we recorded the eye gaze of 90 parents of individuals with ASD and 25 IQ-matched controls as they narrated the wordless picture book *Frog, Where Are You?*. Traits previously described as constituting principal components of the BAP (social features, and rigidity/perfectionistic tendencies) were assessed in parents of individuals with ASD using the Modified Personality Assessment Scale. Percent of time and fixations on areas of interest (i.e., socially salient features, and elements critical to the story's theme) were examined across pages of the storybook and compared across groups.

Results:

Overall, parents of individuals with ASD did not differ significantly from control parents in patterns of fixations throughout their narratives ($p$>.05). However, striking differences emerged in a subgroup of parents who displayed clinically-defined features of the BAP, who spent a lower proportion of time on faces and protagonists, and a greater proportion on inanimate objects, than BAP (-) parents and controls (F=4.056, F=4.951, F=4.810 all $p$s<.025).

Conclusions:

To our knowledge this study is the first to explore perceptual processing patterns during narration. Consistent with previous findings, results suggest that subtle differences in visual attention to social stimuli may be an index of genetic liability in ASD. Notably, our results also suggest that differences in perceptual processes may be specific to those parents showing clinical features of the BAP. Discussion will focus on the potential of gaze as an endophenotype in ASD as well as the complex relationship between perceptual processes and social and language features of the BAP.

**118.056 56** Taxonomic Categorization in Children with High-Functioning Autism Spectrum Disorder. K. Wright*[1], D. Poulin-Dubois[1] and E. A. Kelley[2], (1)*Concordia University*, (2)*Queen's University*

Background: Taxonomic categories can be formed at different levels of inclusiveness. Basic-level categories contain the most within-class similarity of local details (e.g. cats vs. dogs), while superordinate level categories contain less similarity (e.g. animals vs. vehicles); finally, animate-inanimate level categories have the least within-class similarity (e.g. animates: people and animals vs. inanimates: vehicles and furniture). Few studies have examined the formation of these categories in children with autism.

Objectives: to examine taxonomic categorization in typically developing (TD) children and children with high-functioning autism (HF-ASD) across varying levels of category inclusiveness. The weak central coherence account would suggest superior performance on categorization tasks requiring attention to local details (e.g. basic-level categories), as well as difficulty on tasks requiring the ability to extract broader, more conceptual concepts (e.g. animate-inanimate categories).

Methods: Categorization at three levels of inclusiveness was tested using the matching-to-sample and object sorting procedures. In the matching-to-sample procedure, a sample and two comparison pictures were presented and children were instructed to touch the picture that is "the same kind of thing." A proportion of correct responses was computed for each category level. In the object sorting procedure two sample objects were placed in transparent plastic bowls and children categorized a set of new objects by placing each in the bowl with "the same kind of thing." On this task, taxonomic categorization yielded a maximum score of 4.

Participants: 22 children with HF-ASD were matched with 21 TD children on non-verbal

mental age (Differential Abilities Scale, Second Edition), *M* = 6.73 years, *p* = .97 and chronological age, (*M*= 7.15 years), *p* = .34. All diagnoses for children with ASD were confirmed using the Autism Diagnostic Observation Schedule (ADOS).

Results: Children with HF-ASD performed similarly to TD controls across categorization levels on the matching-to-sample task. However, both groups performed more poorly on animate-inanimate trials, compared to the superordinate and basic levels. On the object sorting task, the two groups performed differently across levels, whereby children with HF-ASD and TD controls performed similarly on basic and superordinate level categorization, but children with HF-ASD tended to perform better on animate-inanimate trials (*M* ASD = 2.86, *M* TD = 1.91), *p* = .07. This group effect was due to TD children creating thematic associations when forming object groups (e.g. putting people on the furniture, or inside the vehicles).

Conclusions: No evidence for enhanced basic-level categorization or autism specific deficits in animate-inanimate categorization was found. Thus, the profile of categorization abilities demonstrated by children with HF-ASD did not fit the expected profile based on the weak central coherence hypothesis. Interestingly, children with HF-ASD maintained a taxonomic categorization strategy on the object sorting task, while TD children more flexibly adopted both taxonomic and thematic categorization strategies, reflecting the typical deficit in playful pretense observed in ASD children.

**118.057 57** The Executive Function Challenge Task (EFCT): Development of a Lab-Based Observational Measure for Flexibility and Planning in Children with ASD. L. G. Anthony*[1], J. F. Strang[1], C. Luong-Tran[1], M. A. Werner[2], A. C. Armour[1], K. K. Powell[3] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*Ivymount School*, (3)*Yale Child Study Center*

Background:

Parents, teachers and clinicians of children with ASD have observed cognitive and behavioral flexibility and planning deficits that inhibit the child's ability to socialize and complete every day tasks. Recent reviews of the literature revealed that it is very difficult to capture these observed executive functioning (EF) deficits with laboratory measures. To date, an observational measure that is sensitive to core EF difficulties and capable of tracking improvements in children with ASD has not been developed.

Objectives:

Design an ecologically-valid, well-controlled observational measure that captures difficulties, strengths and change in EF, particularly flexibility and planning, in verbal children with ASD.

Methods:

Sixty-two children with ASD ages 8-12 (Mean=10.31,SD=1.0) without ID (IQ>70) participated in the study. Fifty-five of the children were males (88.7%) and were: Asian 16.1%, Black 11.3%, Hawaiian/Pacific Islander 3.2%, White 64.5% and Other 4.8%. The data were collected as part of a comparative effectiveness treatment study.

The EFCT is a 30-minute interview that challenges children to be *flexible and planful* in the context of five activities. Each task is standardized with specific verbal instructions that are provided by the examiner and explicit guidance about what prompts can be given in response to the child's actions. Scoring criteria are also standardized. Specific challenges to the child's flexibility and planning are introduced in each task (e.g. in one task the child is told that the time is up and they have to clean up a puzzle before it has been completed, in another the child is asked to explain the steps he/she will take to make a clay sculpture).

The EFCT yields average Flexibility and Planning scores and an overall rating of Social Appropriateness. Examiners achieved inter-rater agreement >90%. Scores on the EFCT were compared to lab measures completed by a different examiner (subtests on the Wechsler Abbreviated Scale Intelligence (WASI), the ADOS Restricted/Repetitive Behaviors/Interests (RRBI), Delis Kaplan Executive Function Scale Category Fluency/Switch Contrast score (DKEFS)), parent report measures (Behavior Rating Inventory of Executive Functions, a longer EF questionnaire, Social Responsiveness Scale) and classroom observations.

Results:

EFCT Flexibility correlates with WASI Block Design (r=-.387,p<.01), ADOS RRBI (r=.277,p=.03), DKEFS (r=-.261,p<.05), parent report of EF problems (r=.296, p=.05), and amount of interference from EF problems (r=.281,p=.03). EFCT Planning correlates with WASI Block Design (r=-.318,p=.01), WASI Similarities (r=-.280,p=.03), and Following Rules in the classroom observation (r=.272,p=.03). EFCT Social relates only to parent report of EF problems (r=-.391,p=.01). The EFCT has also been demonstrated to be sensitive to treatment effects (Kenworthy and Anthony et al., in press).

Conclusions:

Our findings suggest that the EFCT is sensitive to difficulties, strengths and change in EF skills. As there are some relationships with both lab-based and "real world" measures, we see the EFCT as a potential bridge between these methodologies to accurately measure change in core EF deficits over time in an ecologically-valid measure. The relationships presented here, though significant, are not large effects, suggesting that the EFCT is capturing a unique set of behaviors that could be important in future treatment research efforts.

**118.058 58** Using the Autism-Spectrum Quotient and Social Network Size to Investigate Individual Variability in Social Attention in the Typical Population. D. A. Hayward* and J. Ristic, *McGill University*

**Background:** It is well documented that gaze direction causes shifts of attention. However, it remains unclear whether this attentional effect relates to social functioning in daily life. Data with clinical populations (i.e., individuals with autism spectrum disorder; ASD) suggest that a reduced interpretation of the social meaning of gaze in individuals with ASD might result from their susceptibility to irrelevant perceptual changes in the environment like pupil motion, which often accompany gaze shifts. Thus, typical individuals who are less socially competent might also be more susceptible to irrelevant changes in the perceptual environment, which in turn may reduce their ability to attend to a social gaze cue. **Objectives:** Here we investigated whether task irrelevant perceptual changes differentially affected attention to social gaze information as a function of individual level of social functioning. **Methods:** Thirty-nine undergraduate students completed: (i) a gaze cuing task, in which an irrelevant perceptual change entailed presenting gaze cues as either an onset or an offset; (b) the Autism-spectrum quotient questionnaire, which measures social competence in typical populations; and (c) the Social network questionnaire, which measures social network size. **Results:** Performance of socially competent participants did not vary with the tasks' perceptual changes. However, in agreement with clinical data, less socially competent participants showed reduced magnitudes of social orienting when the task contained an irrelevant perceptual change, i.e., when cue onset and offset trials alternated. Furthermore, their scores on both questionnaires accounted for a significant amount of variability in their social orienting magnitudes under conditions of perceptual change. **Conclusions:** These data link social attention and social functioning and show that performance of typically developing individuals with lower social competence mirrors performance measured in clinical populations.

**118.059 59** Visual Attention to Faces Is Related to Social Referencing: A Study of 16-Month-Old Infants at High and Low Risk for Autism. L. Sperle*, M. S. Strauss and S. B. Campbell, *University of Pittsburgh*

Background: To understand the origins of autism spectrum disorder (ASD) and allow for earlier diagnosis, research has examined infants who are at heightened genetic risk based on their having an older sibling with ASD. Up to 20% of infant-siblings may later receive an ASD diagnosis (Ozonoff et al., 2011). We focus on lower levels of social interest across contexts as possible early signs of ASD. Social referencing requires infants to distribute their attention between an object of interest and a social partner, but few prospective studies have investigated early social referencing deficits in ASD (Cornew et al., 2012). Moreover, no studies have examined how underlying attentional demands relate to social referencing.

Objectives: The current study investigated visual attention and social referencing among 16-month-old infants with (high-risk, HR) and without (low-risk, LR) an older sibling with ASD. We also examined whether visual attention differences (e.g., attention to faces during a videotaped social scene from Mr. Rogers) were related to variability in social referencing. It was expected that HR infants would demonstrate less visual attention to faces and lower rates of social referencing compared to LR infants, and that visual attention differences to dynamic social scenes would be

associated with lower rates of social referencing during the naturalistic interaction.

Methods: A prospective study design was used to compare HR infants ($n$=36) with LR infants ($n$=33). Eye-tracking data were collected while 16-month-olds viewed a dynamic social scene of an adult (Mr. Rogers) speaking and showing toys. These same infants also participated in a social referencing paradigm in which the infant was introduced to an appealing but somewhat frightening novel toy in the presence of an experimenter and caregiver.

Results: During the dynamic social scene, HR infants spent a lower proportion of time looking at the upper half of the face ($M$=.13, $SD$=.23) compared to LR infants ($M$=.27, $SD$=.28) ($F$(1, 51)=4.46, $p$=.04, partial $\eta^2$=.08). HR infants also referenced the adults less frequently ($M$=1.69, $SD$=1.45) than did LR infants ($M$=2.71, $SD$=2.37) ($F$(1, 67)=4.72, $p$=.03, partial $\eta^2$=.07). In addition, infants who spent more time looking at the upper half of the face during the social scene were also more likely to reference an adult when shown the ambiguous toy ($r$=.35, $p$=.03). In contrast, a higher proportion of looking time to the objects was associated with lower rates of social referencing ($r$=-.31, $p$=.04).

Conclusions: High risk infants showed lower social interest as reflected in both less visual attention to the upper half of the face and less social referencing at 16 months of age. Importantly, attention to the upper half of the face was positively associated with social referencing, whereas attention to objects was negatively correlated with social referencing. This study is the first to report an association between visual attention to faces and objects and social referencing during social interaction. Further research is needed to understand how these measures relate to other indices of social interest and engagement and whether they will prove to be useful early signs of ASD.

**118.060 60** Visual Function in Adults with High Versus Low Autism Quotient Scores. V. L. Armstrong*[1], F. Tremblay[2] and S. E. Bryson[3], (1)*IWK Health Centre*, (2)*Dalhousie University*, (3)*Dalhousie/IWK Health Centre*

Background: Although hyper- and hypo-sensitivities to various forms of sensory input are commonly reported in individuals with autism spectrum disorder (e.g., Iarocci & McDonald, 2006), it remains unclear how or why these problems occur.

Objectives: Our goal is to determine whether there are differences in sensory processing in people with high- versus low-levels of autistic-like traits. In the current study, we focus on vision. Research implicates visual differences between people with and without autism spectrum disorder (ASD), although results are equivocal (see Simmons et al., 2009 for review). By assessing vision in typical adults with high- and low-levels of autistic-like traits, we hope to circumvent problems associated with studying people with ASD, including small sample sizes and various confounds.

Methods: Participants were adults aged 18-29 years. Each participant completed an online survey: The Autism Quotient (AQ). Participants with the highest and lowest 10% of AQ scores were invited to participate in two lab-based sessions. To date, 13 low AQ ($M$= 8.0, $SD$=2.3) and 18 high AQ individuals ($M$=31.0, $SD$=5.0) have been seen. Participants reported no history of visual problems. Visual screening showed no group differences in logMAR acuity, stereoacuity on the Titmus test, nor fusion on the Worth 4 dot test. In the first session, participants completed the Dunn Sensory Profile and the Broad Autism Phenotype Questionnaire (BAPQ). We also measured participants' sensitivity to form and motion using psychophysical threshold tasks. Tasks included first-order local motion and pattern discrimination, second-order local motion and pattern discrimination, glass patterns (global form discrimination) and random-dot kinematograms (global motion discrimination). These tasks target lower- and higher-levels of the dorsal and ventral pathways of the visual system. In a separate visit, visual evoked potentials (VEPs) were recorded from each participant in response to pattern reversals and motion onset.

Results: AQ scores correlated strongly with BAPQ scores, $r$(30)=.76, $p$< .001. Scores on the Dunn Sensory Profile differed between the high and low AQ groups. Specifically, the high AQ group was both more hypo- and hyper-sensitive to sensory information ($p$'s<.05 and .001, respectively). The high AQ group also had higher levels of sensory avoidance behaviour ($p$<.001) and lower levels of sensory seeking behaviour ($p$<.01). In contrast, we found no group differences in sensitivity to

form or motion using threshold tasks. Preliminary analyses of VEPs showed group differences in response to motion onset but not pattern reversal. Specifically, for motion onset, the high AQ group had reduced peak amplitude for the N2 waveform.

Conclusions: We show that typical adults with autistic-like traits have sensory processing styles similar to people with ASD (Crane et al., 2009). VEPs suggest group differences in the processing of motion, but not pattern. Group differences were not large enough to be evident using threshold tasks, at least under the tasks demands of the current study. It is possible that the equivocal findings of atypical vision in ASD reflect task difficulty and/or subtle differences in visual processing that are difficult to measure in high functioning people with ASD or typical adults with autistic-like traits.

## 119 Communication and Language

**119.061 61** A Cross Cultural Look at Parenting Beliefs about Child Rearing and Verbal Interaction with Their Children with Autism Spectrum Disorders. V. Smith*, *University of Alberta*

Background:

According to best practice guidelines for treating children with autism spectrum disorders (ASD), including and training parents to assist their child's communication development is considered an essential component and a natural step to provide consistent, daily support in early childhood. Research suggests that parents can learn to be effective language facilitators; however, we know very little about the cultural differences, including beliefs and practices, of parents of children with ASD. In fact, the sporadic observations of non-Western cultural groups have made it clear that the large literature on language facilitation strategies primarily describes Western parent-child interaction patterns.

Objectives:

The aim of the present study was to 1) review the literature on early parent-child interaction across cultures for typically developing children and for children with ASD. This review served as the basis of a questionnaire that was developed 2) to better understand parents' beliefs about child rearing and 'how to talk to children' to promote language development in four cultural groups of parents of children with ASD: South Koreans, South Indians, Euro-Canadians, and Indo-Canadians.

Methods:

Items in the questionnaire were designed in consultation child language scholars, speech and language pathologists, health care workers from both Korea, Indian, and Western cultural groups and addressed: independence of child's learning, nature of language learning, and early language milestones, beliefs about disability, and parenting. The questionnaire was administered to 128 South Korean, 71 Indian families of children with ASD and contrasted with 65 Euro-Canadian and Indo-Canadian families of children with ASD.

Results:

Differences across the four cultural groups were found in aspects of socialization, the value of talk, beliefs about disability, the way status is handled in interaction, and understanding about teaching language to children.

Conclusions:

Interpretation of the findings was made by attempting to understand the cultures and their implied values and beliefs. Family functioning has a huge impact on the effectiveness of interventions and so too do their cultures. The beliefs and values that inform family functioning influence the creation of each child's unique 'developmental niche;' thus better understanding of culture may helps us to design interventions that are applicable to families of diverse cultural back grounds.

**119.062 62** A Fine-Grained Analysis of Longitudinal Language Use in Toddlers with ASD: The Case of GAP Verbs. J. Parish-Morris*[1], C. Gilman[2], D. A. Fein[3] and L. Naigles[3], (1)*University of Pennsylvania*, (2)*The Children's Hospital of Philadelphia*, (3)*University of Connecticut*

**Background:** Language delay is a primary concern for many toddlers with ASD (DeGiacomo & Fombonne, 1998), and the presence of language before age 5 in this population is a powerful predictor of functional outcome (Anderson et al., 2009). Research using parent-report measures suggests that vocabulary in ASD is delayed but not deviant in composition (Rescorla & Safyer, 2013), but little is known about word use in the real world, and even less about the productive lexicon over time. Although prior research has examined word classes at a gross level (e.g., proportion of nouns versus

verbs; Tek et al., 2013) no studies to date have taken a fine-grained approach to productive language by measuring not only *if* children use words from a given class, but also *which* words are used *when* and *how*. The present research fills this gap by exploring two kinds of verbs: content verbs (Content; e.g., *bite, juggle*) and general all-purpose verbs or light verbs (GAP; e.g., *go, want*). GAP verbs are used more often in typical speech than content verbs, but these verbs have never been explored in toddlers with ASD.

**Objectives:** Characterize the developing nature of GAP and Content verb use in typical toddlers (TD) and toddlers with ASD. Given that the overall proportion of verbs to nouns is similar in language-matched ASD and TD children, and these children learn language via many common mechanisms, we hypothesize that children with ASD, like TD, will rely more on GAP verbs than Content verbs over time.

**Methods:** Seventeen toddlers with ASD (mean age=32.86 months) were matched to 18 TD toddlers (mean age=20.60 months) on Expressive and Receptive Language abilities (MSEL) at Visit 1 of a 6-visit longitudinal study. The language produced by parents and children during three 30-minute semi-structured home-based play sessions (each 8 months apart; i.e., Visits 1, 3, 5) was recorded and transcribed in CHAT format.

**Results:** Growth curve analyses using linear mixed models revealed that change in the proportion of GAP verbs used by children over time did not differ by group (all $p>.10$). The average number of times each GAP verb was used (tokens/types) grew more steeply in TD than ASD ($t=2.72$, $p=.009$). This is likely due in part to lower rates of GAP verb use in the TD group at Time 1, and consistently high average usage of GAP verbs in the ASD group.

**Conclusions:** Toddlers with ASD and TD show similar patterns of GAP and Content verb use in a naturalistic play interaction. This analysis represents the first foray into a rich dataset that can answer a number of questions, including: which words within a class do toddlers with and without ASD actually use, and how do they use them? Do subgroups within ASD use different words, or use the same words differently? Future growth curve analyses will be conducted on verbs of communication (e.g., *ask, say*), internal state verbs (e.g., *see, think*), action verbs (e.g., *jump, fall*), and social verbs (e.g., *share, help*) across all 6 available time points.

**119.063 63** An Exploration of the Phenotypic and Etiological Relationships Between Autism Spectrum Disorder and Specific Language Impairment. L. J. Taylor*[1], M. T. Maybery[2] and A. Whitehouse[3], (1)*Telethon Institute for Child Health Research*, (2)*University of Western Australia*, (3)*Telethon Institute for Child Health Research, The University of Western Australia*

Background: While Autism Spectrum Disorder (ASD) and Specific Language Impairment (SLI) have traditionally been considered as distinct disorders, evidence is emerging which indicates that the boundaries between the two conditions are not clear-cut. Specifically, findings that a subgroup of children with ASD has structural language difficulties similar to those observed in SLI have led some authors to claim that there is substantial aetiological overlap.

Objectives: Much of the research to date has focused on overlap in the language phenotypes of ASD and SLI and no previous study has investigated potential cognitive overlap. Therefore, the aim of this study was to examine possible points of cognitive similarity in children with ASD, children with SLI, and the parents of both groups of children.

Methods: 32 Children with an ASD (18 with 'normal' and 14 with 'impaired' language), 19 children with SLI and 61 typically developing (TD) children completed tasks that tapped phonological working memory (nonword and sentence repetition), a known deficit in SLI, and tasks that measured cognitive characteristics of ASD, namely 'weak central coherence' (assessed by the Children's Embedded Figures Test: CEFT) and emotion recognition ability.

We also examined possible shared heritable risk factors for ASD and SLI. 24 ASD parents, 12 SLI parents and 20 parents of TD children completed measures sensitive to the broader SLI (nonword and sentence reptition) and broader ASD (Embedded Figures Test, emotion recognition task) phenotypes.

Results: 'Language impaired' children with ASD and children with SLI performed worse than both 'language normal' ASD and TD children on the nonword and sentence repetition tests. In

addition, the SLI children performed worse than all other groups on the CEFT. For the emotion recognition task, all clinical groups were less accurate than the TD children across visual and auditory domains. The only significant group differences that emerged for the parents were on the nonword repetition task (ASD parents were worse than the SLI and the TD parents) and the emotion recognition task (ASD parents were faster than the SLI parents and less accurate than the TD parents).

Conclusions: These findings point to areas of overlap, as well as points of divergence in the cognitive profiles of ASD and SLI, and the heritable phenotypes of these conditions. The results have implications for the debate about aetiological overlap in ASD and SLI.

**119.064 64** Sticky Attention and Word Learning in Children with ASD. C. E. Venker*[1] and S. Ellis-Weismer[2], (1)*Waisman Center, University of Wisconsin-Madison*, (2)*University of Wisconsin-Madison*

Background:

Children with ASD demonstrate atypical patterns of attention that may impact language development. One of the most striking and earliest emerging differences seen in ASD is difficulty disengaging visual attention from a salient stimulus—a phenomenon known as sticky attention (Landry & Bryson, 2004). Sticky visual attention may negatively affect children's abilities to switch attention among multiple candidate word referents, which is a requirement for successfully extracting co-occurrence statistics from ambiguous contexts (i.e., cross-situational word learning; Smith & Yu, 2008).

Objectives:

The primary objective of this study was to determine whether stickier attention (i.e., longer latency to disengage) was associated with poorer performance in a cross-situational word learning task. A secondary objective was determining the specificity of this relationship. It was hypothesized that sticky attention, but not overall shifting speed, would relate to cross-situational word learning in the children with ASD but not in the typically developing (TD) children.

Methods:

Participants were 20 children with ASD (4 – 7 years) with heterogeneous language and cognitive abilities, and 27 TD children (2 – 7 years) matched on receptive vocabulary. Children in the ASD group had a community diagnosis of ASD and diagnoses were confirmed through administration of the ADOS. Children participated in a cross-situational word-learning task presented on an eye tracker that required attention to the co-occurrences between words and objects across individually ambiguous trials. In the test phase, children were asked about one of the novel words they had learned (e.g., *Where's the coro*?). Accuracy was measured by the proportion of looks to the correct image during the test phase. Children also participated in a non-social eye-gaze task that measured latency to shift and disengage attention. In the disengage condition, children saw two competing stimuli. In the shifting condition, stimuli were not competing.

Results:

Mean latency to shift was 0.52 seconds in the TD group and 0.81 seconds in the ASD group. Mean latency to disengage was 2.27 seconds in the TD group and 1.67 seconds in the ASD group. Contrary to previous findings, the ASD and TD groups did not differ in mean latency for disengagement or shifting of attention, $p > .95$; latencies were longer for disengagement than for shifting.

Consistent with predictions, sticky attention (i.e., longer latencies to disengage) was negatively associated with cross-situational word learning, $r = -.43$, $p = .03$ (one-tailed). This relationship was non-significant in the TD group, $p = .20$. Shifting speed was not significantly correlated with cross-situational learning in either group, $p$s $> .60$, pointing to a specific role of visual disengagement.

Conclusions:

Sticky attention was related to cross-situational word learning in children with ASD. This finding is important because it demonstrates the negative impact of sticky attention—an early-emerging and atypical feature of ASD—on a specific type of word learning. Differences in disengagement of visual attention may help to explain delays in vocabulary learning and language processing. Future work

will focus on the impact of sticky attention on moment-to-moment patterns of eye gaze.

**119.065 65** Does Gender Moderate Core Deficits in ASD? an Investigation into Social-Communication and Play. C. Harrop*[1], A. Gulsrud[2], Y. C. Chang[2], E. H. Ishijima[1], K. Lawton[3], S. Patterson[1] and C. Kasari[1], (1)*University of California Los Angeles*, (2)*UCLA*, (3)*Nisonger Center*

Background: Due to the male dominance in ASD (Brugha et al., 2011; Kim et al., 2011), girls are rarely studied independently. Therefore our understanding of the behavioral phenotype of females with ASD is still limited. It is has been suggested that girls with ASD require a greater symptom "threshold" to reach diagnosis possibly leading to later detection (Dworzynski et al., 2012); however an interaction with intellectual disability potentially makes girls more likely to fall at the severe end of the spectrum (Carter et al., 2007; Fombonne, 2003). In terms of phenotypic profiles, research surrounding girls with ASD girls is extremely varied with some studies suggestive of superior social abilities in early childhood (Kopp and Gillberg, 1992) and others indicative of matched abilities relative to boys (Andersson et al., 2013).

Core deficits in social-communication and play behaviors are extensively reported in children with ASD and frequently targeted through intervention (e.g., Kasari et al., 2006). In typical development, girls are known to display early advantages in social-communication and play behaviors, however we do not know whether girls and boys with ASD differ on the specific behaviors of initiating joint attention (IJA), initiating behavioral requesting (IBR) or play in early childhood.

Objectives: We were interested in whether girls demonstrated superior social-communication skills in early childhood compared to boys. We also examined whether gender moderated the effect of developmental variables on social-communication and play diversity.

Methods: 40 girls with ASD (*mean* CA: 40m) were individually matched to 40 boys based on ADOS module and severity score. The two groups were not purposefully matched on MSEL DQ or CA, but did not differ on these variables. Their play complexity was also matched. All children completed measures of early social-communication (ESCS: Mundy et al, 2003) and play (SPA: Ungerer & Sigman, 1981).

Results: Girls and boys did not differ in the number of novel acts produced ($t$ (78)= -1.19; $p$ = .24). While girls did initiate joint attention and behavioral requests more than boys, these differences were not significant.

We ran separate ANCOVA models with gender as a predictor while co-varying for various developmental variables. Gender produced significant main effects on IBR when developmental variables were controlled (CA, expressive and receptive language) but not NVIQ. A significant interaction was found between gender and CA on IBR ($F$ (3,1) = 4.70, $p$ = .03). These effects were not found for IJA or play.

Conclusions: Overall girls and boys in our sample were more similar than dissimilar supporting recent findings (Andersson et al., 2013). Gender interacted with both chronological age and language abilities for IBR acts. This interaction was moderated by the boys; girls did not improve in their IBR with age or development. Interactions with developmental variables were not found for IJA or play, suggestive of a unique gender role in requesting. Whilst our data is cross-sectional, it is to our knowledge the largest sample of girls studied behaviorally to date and raises interesting questions as to whether one should approach requesting within intervention differently for girls.

**119.066 66** Children's Use of Disfluencies Distinguish ASD and Language Impairment. K. Gorman*, S. Bedrick, R. Lunsford, P. Heeman, L. Olson, G. Keepers, E. Fombonne and J. van Santen, *Oregon Health & Science University*

Background: Deficits in social communication, and pragmatic language in particular, are characteristic of individuals with autism spectrum disorders (ASD). The filled pause markers "uh" and "um" play a subtle role in shaping discourse; they are not merely speech errors. Filled pauses (FPs) provide valuable cues to the listener and are used to signal uncertainty, speech repairs, production difficulties, and to negotiate control of the floor. Typically developing children are thought to be sensitive to these cues and their meaning as early as age two. Children with ASD who are verbal are also known to use filled pauses conventionally, i.e., to signal production difficulties. "Um" is thought to play a larger role in shaping discourse, and its use to be under conscious control; "uh" is less salient, and its use is largely automatic. Given this, we hypothesized that communication impairments in children with

ASD would selectively spare "uh" but produce lower rates of "um".

Objectives: This study compares the relative frequencies of "uh" and "um" in the spontaneous speech of children with ASD (with or without comorbid language impairment) to two control groups.

Methods: Participants: 112 children ages 3;10–9;0 participated: ASD (50), Specific Language Impairment (SLI; 18), and Typical Development (TD; 44). All diagnoses were verified by best-estimate clinical consensus. The children with ASD were split into two groups: one group with comorbid language impairment (ALI) as diagnosed by a CELF Core Language Score below 85, and one group with ASD but no clinical language impairment (ALN). All children were high functioning monolingual English speakers. Data collection: a clinician administered the Autism Diagnostic Observation Schedule (ADOS; module 2 or 3) to each child. Sessions were recorded and transcribed. Software was used to count each child's FPs; 4,067 FP tokens were collected in all. Group matching: All groups were matched on chronological age. The ALI/ALN group pair was also matched on ADOS severity score and Social Communication Questionnaire score. The ALN/TD and ALI/SLI group pairs were also matched on PIQ and VIQ.

Results: For all group pairs, diagnosis was uncorrelated with overall (i.e., "uh" + "um") rate of filled pause use. FP choice was analyzed for each comparison set using mixed effects logistic regression, with chronological age, FSIQ, ADOS "activity", and utterance position (utterance-initial vs. non-initial) as covariates. Diagnosis was a significant predictor for ALN/TD ($p = .001$) and ALI/SLI ($p = .038$); in both comparisons the ASD group used fewer instances of "um". Diagnosis was non-significant for TD/SLI ($p = .888$) and ALI/ALN ($p = .814$). ALI and ALN groups both used "uh" and "um" at an approximately 1:1 ratio, whereas TD and SLI groups used "um" 2 to 3 times more often than "uh". ADOS "activity" and utterance position were also significant predictors of FP choice; remaining covariates were non-significant.

Conclusions: The relative use of "uh" and "um" in spontaneous speech is highly sensitive to ASD diagnostic status, but insensitive to language impairment. This provides clinicians with a novel feature distinguishing ASD and SLI, a notoriously difficult differential diagnosis.

**119.067 67** Exploring the Narrative Writing Skills of Students with High-Functioning Autism Spectrum Disorders. H. M. Brown*[1], J. Oram Cardy[1], R. E. Smyth[1] and A. Johnson[2], (1)*Western University*, (2)*Western University, Canada*

**Background**: No genre is as dependent on social cognition as the narrative genre. For students with autism spectrum disorder (ASD), core weaknesses in social understanding and communication could make writing narratives one of their most challenging academics areas. Despite this, no studies to date have examined the narrative writing skills of children and adolescents with ASD, beyond a few using standardized tests that suggested global writing deficits in this population. Furthermore, previous research has confounded language ability with a diagnosis of ASD. Systematic description of the strengths and weaknesses in the narratives of students with ASD is critical to disentangling oral language impairments from autism within the writing problems of students with ASD, and this is critical in providing a foundation for developing targeted interventions.

**Objectives**: The aim of this study was to compare the narrative writing of students with ASD to their typically-developing (TD) peers when both groups were balanced in terms of language ability. We hypothesized that ASD would contribute to written language strengths and weaknesses beyond what would be predicted by oral language skill alone. A second aim was to explore the variables that best predicted writing quality across both groups.

**Methods**: Twenty-four students with ASD and 22 TD controls aged 8 to 17 years participated in this study. Participants completed standardized assessments of oral language skill, performance IQ, and ASD symptomology, as well as an untimed narrative writing task. Their narratives were coded on 20 text variables across four lower order categories: productivity, syntactic complexity, lexical diversity, and writing conventions, as well as two higher order composites: overall narrative clarity and overall narrative quality.

**Results**: Omnibus MANCOVA (controlling for age) revealed that the students with ASD showed

greater lexical diversity in their texts compared to their TD peers ($d$ = +0.9 SD). ANCOVA revealed that the texts of students with ASD had lower overall narrative quality than controls ($d$ = -0.7 SD). The groups did not differ significantly on any other variables. Forward multiple regression revealed that age, language ability and ASD symptomology (but not PIQ) were significant predictors of overall narrative quality ($R^2$=.557).

**Conclusions**: This was the first detailed investigation of the narrative writing skills of students with ASD and the first to ensure both groups were equivalent on language ability. Results revealed many similarities in the texts of students with ASD and controls. However, individuals with ASD tended to have difficulty with their use of narrative elements and form, i.e., problems with narrative structure and organization, character development and integrating the inner worlds of their characters with the events in the story.

We theorized that individuals with ASD may have underdeveloped narrative concepts and structures, and that they may engage in narrative thought less often. Providing repeated opportunities for youth with ASD to engage in narrative thought, such as through the creation of written narratives, could help them to better understand human acts and events. As such, developing interventions to support the narrative abilities of students with ASD may have far-reaching consequences.

**119.068 68** Responsiveness to Children's Gestures Facilitates Word-Learning in Children with Autism. N. Dimitrova*, S. Ozcaliskan and L. B. Adamson, *Georgia State University*

Background: At the one word-stage, typically developing (TD) children often produce gestures conveying unique information not found in the accompanying speech (e.g., "eat"+point at cookie); and parents provide labels for the referents indicated in gesture, translating their children's gestures into words. Importantly, approximately 75% of the referents children convey uniquely in gesture, when explicitly labeled by the parent, enter the child's productive vocabulary (Goldin-Meadow et al., 2007).

Objectives: Here we ask whether this pattern of findings holds true for children with autism spectrum disorder (ASD), who show difficulties in early gesture production. One possibility is that parents of children with ASD will be as likely as parents of TD children to rely on their children's gestures and thereby provide verbal labels that match their child's own gesture production. Another possibility is that parents of children with ASD might be less likely to rely on children's gestures given early deficits that children with ASD show in gesture production.

Methods: To test these possibilities, we observed 23 children with ASD, from 30- to 42-months of age, as they interacted with their mothers for 20 minutes in a semi-naturalistic laboratory setting. We assessed children's gestures conveying unique information not found in the accompanying speech and we compiled children's gesture vocabulary, i.e. a list of objects children referred to only in gesture. We then examined whether parents translated those referents into words. Additionally, we assessed children's subsequent productive vocabulary during the observation sessions at 33, 36, 39, and 42 months of age for the referents children indicated uniquely in gesture at 30 months.

Results: Preliminary analyses of a subset of our sample reveal that, when children used gesture, they frequently conveyed unique information not found in the accompanying speech (78% of the gestures produced by TD children and 73% of the gesture production by children with ASD). For both groups, mothers translated approximately 50% of the referents conveyed uniquely in gesture, providing their children with labels for the objects. Importantly, 41% and 64% of the referents that the mothers translated into speech entered the spoken vocabulary of TD children and children with ASD, respectively.

Conclusions: These results show that parents of children with ASD are as responsive to their children's gestures as parents of TD children in providing contingent spoken language input for children's subsequent vocabulary development. Children with ASD, in turn, benefit from this targeted input, acquiring words that their parents translated at an earlier age. Overall, our results extend to children with developmental disorders the important role that children's gestures play in language development—largely through its effects on parental responsiveness to these gestures.

**119.069 69** Eye-Tracking Measurements of Language Processing: Developmental Differences for Infants at High Risk for

Autism. M. Chita-Tegmark*[1], C. A. Nelson[2] and H. Tager-Flusberg[1], (1)*Boston University*, (2)*Boston Children's Hospital*

Background:

Children with ASD have impaired online processing of language, a predictor for later language development (Venker, Eernisse, Saffran & Weismer, 2013). Since in some aspects of their development, children at high risk for autism (who have a sibling with ASD) are more similar to children with ASD, and in others are more similar to typically developing children, this study investigates which of the two is true of online language processing.

Objectives:

Three components of online processing of language were explored: *comprehension* (measured through accuracy and reaction time), *sustained attention* (to the language input as well as to the language referent), and *visual reception* (of the referent associated with the spoken language).

Methods:

A paradigm similar to that of Fernald and colleagues (2006) was used to investigate online speech processing at three different ages: 18, 24 and 36 months. 125 children participated in the study, 57 children at high risk for autism and 68 children at low risk. 16 children from the high-risk group were diagnosed with autism at 36 months, and their data was analyzed separately.

In each session, a child saw 20 image pairs, 10 depicting early acquired nouns and 10 depicting later nouns. A blank screen was shown for one second, followed by a pair of pictures that the child was allowed to explore freely for three seconds, after which a recorded voice instructed the child to *"Look at the (target noun)*!". The pictures remained on the screen for two additional seconds. For higher time resolution, and in order to circumvent coder reliability issues, we used not a camera but an automated infrared eye-tracker, the TOBII T60, to acquire the gaze data.

Results:

After noun onset, the percentage of trials in which the children were looking at the target image as opposed to the distractor image was calculated as a function of time.

The results show that children at high risk for autism demonstrate significantly lower accuracy (percentage looking at target image) than the low risk children for later developing words at 36 months ($p=0.02$) but not for early developing words. Also, at 36 months, low risk children show a significantly better sustained attention to the target image than children at high risk for autism ($p<0.001$). Performance on the eye-tracking task is significantly correlated with the visual reception skills as measured by the Mullen test at 36 months for the high-risk children ($p=0.005$), but not for the low-risk children. The results for children with ASD show a similar pattern to those of children at high risk.

Conclusions:

Performance on this eye-tracking language task captures subtle differences between children at high risk for autism and children at low risk. These differences, which seem to emerge between 24 and 36 months, might have broader and longer-term implications for their development, for example delayed acquisition of spoken language. These differences might also be reflective of social-communicative impairments and the link between performance on this task and visual reception for high risk children might point towards a compensatory mechanism.

**119.070 70** A Quantitative Analysis of Pragmatic Language in Adults with High-Functioning Autism. K. E. Morrison* and L. Wagner, *Ohio State University*

Background: Individuals with autism spectrum disorder often have impaired social communication (DSM-IV-TR; APA, 2000). These deficits, especially in pragmatics (i.e., the rules of conversation) have also been observed in individuals with high-functioning autism (HFA), who possess IQ and verbal skills within the normal range (Baron-Cohen, 1998). While many researchers have observed pragmatic language deficits in individuals with autism, few studies have been conducted in a conversational context.

Objectives: We aimed to identify differences in pragmatic language in conversations between typically developed individuals and individuals with HFA; we hypothesized that the HFA group would have fewer discourse markers, less

supportive interruptions, and more off-topic responses compared to their typically developed peers.

Methods: In two studies, HFA (n=8) and typically developed (n=8) individuals participated in guided discussions that were recorded and transcribed. The data from Study 1 has been analyzed while the data from Study 2 is still being coded.

Results: Discourse markers are words that maintain grounding and listener understanding in conversations (Fox Tree, 2006). For example, the word *like* indicates ambiguity (e.g., they vary in price from five to *like* twenty cents) (Fox Tree, 2006). Usage of the discourse marker *like* was analyzed; preliminary results from Study 1 suggest that typically-developed adults were more likely to use *like*(n=100 times/30 minutes) compared to the HFA adults (n=2 times/60 minutes). Interruption events were analyzed for the outcome (i.e., who won the turn after the interruption), and categorized for their (non-)supportive role in conversation. In HFA speech, the interrupted person regained the turn in 34% of interruption events and the person interrupting regained the turn in 24% of interruption events, whereas in conversations of typically-developed participants, the interrupted person regained the turn in 49% of interruption events, and the person interrupting regained the turn in only 8% of the interrupted events. Moreover, over half of the HFA interruptions were non-supportive, commonly shifting the conversation away from the previous speaker, while over half of the interruptions were supportive in the typically-developed conversations. Lastly, participant responses were coded as appropriate or inappropriate to the topic. Results indicate that the HFA group was off-topic over five times more frequently than the typically-developed group.

Conclusions: These language patterns provide useful information about conversational interaction in adults with HFA, and have potential use for developing interventions to improve social communication skills in these individuals, fostering successful educational and occupational experiences as well as friendships and social competence.

**119.071 71** Does ASD Severity Predict Minimally Verbal Outcome By School Age?. A. Thurm*[1], L. Swineford[2], S. Manwaring[3] and C. Farmer[2], (1)*National Institutes of Health - National Institute of Mental Health*, (2)*National Institute of Mental Health*, (3)*University of Utah*

Background:

A significant minority of children with autism spectrum disorder (ASD) are considered "minimally verbal," characterized by lack of expressive language beyond single words. Although language outcomes have been well-studied, limitations of measures have prevented observationally-based ratings of ASD severity to be explored with respect to the relationship between ASD severity and language through the preschool years.

Objectives:

The goals of this study were to measure expressive language across approximately 2 years in preschool-aged children, and evaluate predictors of language level at age 5 years.

Methods:

Participants were children with DSM-IV diagnosed autistic disorder (n=70) drawn from a larger longitudinal study. Additional inclusion criteria were (a) two study visits at least 11 months apart, and (b) follow-up evaluation between 4 years, 6 months and 6 years, 0 months (inclusive). Study measures included the Autism Diagnostic Observation Schedule (ADOS), used in this study to measure overall level of language (item A1), as well as core deficits of ASD (total and domain severity scores), the Autism Diagnostic Interview-Revised (ADI-R), and the Mullen Scales of Early Learning (used to estimate developmental quotient, DQ). Children were classified as "minimally verbal" if they had no words or some single words based on observation from the ADOS; "verbal" children displayed phrase speech.

Results:

The average age at initial evaluation (Visit 1) was 3.56±0.85 years (range 1.76-4.98); the average time to follow up was 1.90±0.81 years (age range at follow up: 4.62-5.98; mean age: 5.45±0.37). Based on the ADOS item A1, 67% (n=47) of the sample was minimally verbal at Time 1. This group did not differ in age from the verbal group. At Time 2, 36% (n=17 of 47) of those who were minimally verbal at Time 1 had developed phrase

speech. The remainder of analyses focused on the Time 1 minimally verbal subgroup (n=47). Age at Time 1 and time-to-follow-up were not related to minimally verbal status at Time 2 and were therefore excluded from further analyses of predictors. In a logistic regression, Time 1 NVDQ was significantly related to Time 2 minimally verbal status, such that each point of NVDQ at Time 1 conferred a 5% increase in the odds of being verbal at Time 2 (OR = 0.95, $p$<.049). Time 1 VDQ was not significantly associated with Time 2 verbal status (OR=.97, p=.15). ADOS domain calibrated severity scores (Social Affect and Restricted/Repetitive Behavior) did not significantly predict minimally verbal status, with or without NVDQ in the equation.

Conclusions:

The results of this study suggest that although there is growth in expressive language over time through the end of the preschool period, many children with ASD remain minimally verbal entering school age. Consistent with previous findings, NVDQ is a significant predictor of who will develop phrase speech by age 5. ADOS domain calibrated severity scores were not associated with language development, indicating that neither severity of social affect, nor severity of restricted and repetitive behaviors heavily influenced the development of expressive language development during the preschool years.

**119.072 72** Ages of Language Milestones As Predictors of Developmental Trajectories in Young Children with ASD. S. T. Kover* and S. Ellis-Weismer, *University of Wisconsin-Madison*

Background: Recognizing early risk-markers and prognostic indicators in young children with autism spectrum disorder (ASD) is critical for timely diagnosis and intervention (Luyster, Seery, Talbott, & Tager-Flusberg, 2011). Recent studies have identified language milestones, most notably age of first words (Mayo, Chlebowski, Fein, & Eigsti, 2013) and age of first phrases (Kenworthy et al., 2012), to be good predictors of later developmental outcomes. However, previous research has been limited by examination of only a single language milestone, exclusion of children considered to be low functioning or those with a history of regression, and risk of telescoping in parent report for older children (Hus, Taylor, & Lord, 2011).

Objectives: The purpose of the current study was to extend previous findings to a longitudinal design, in which ages of language milestones could serve as predictors of developmental trajectories in a heterogeneous sample of young children with ASD. We hypothesized that age of first word production and, for children for whom these milestones were applicable, age of first phrases and age of regaining babbling after loss would predict level and rate of change for language, nonverbal cognition, and adaptive skills.

Methods: Participants ($N$=98; age in months at first assessment: $M$=31.63, $SD$=4.51) were drawn from a larger longitudinal study on early development in ASD with up to four annual assessments. Age of language milestones was determined by parent report at the initial assessment using the Toddler Research Autism Diagnostic Interview-Revised (LeCouteur, Rutter, Lord, & DiLavore, 2006). Hierarchical linear models were estimated separately for each of four outcome variables, indexing receptive language, expressive language, nonverbal cognition, and adaptive behavior: auditory comprehension and expressive communication standard scores on the Preschool Language Scales-4, Visual Reception T-scores on the Mullen Scales of Early Learning, and adaptive behavior composite standard scores on the Vineland Adaptive Behavior Scales-II.

Results: Age of first words positively predicted rate of change for adaptive behavior, $t$(96)=2.04, $p$=.045. For the 30 participants with phrases, age of first words negatively predicted level of expressive language, controlling for age of first phrases, $t$(27)=-2.19, $p$=.037. Age of first phrases was not a significant predictor for any outcome. For the 26 participants who had lost and regained babbling, age of regaining babbling negatively predicted level of receptive language, $t$(23)=-2.42, $p$=.024, expressive language, $t$(23)=-2.93, $p$=.008, and nonverbal cognition, $t$(21)=-2.10, $p$=.048, controlling for age of first words. Age of first words was not a significant predictor for any outcome for this subgroup, controlling for age of regaining babbling.

Conclusions: Age of first words predicted trajectories of expressive language and adaptive skills, but not receptive language or nonverbal cognition. Young children with earlier first words

had higher levels of expressive language; those with later first words made faster gains in adaptive skills. Prognostic indicators other than first words, such as age of regaining babbling, may be important for children who have experienced babbling regression. Ages of some language milestones relate to developmental trajectories and may help define when immediate intervention is justified, with implications for service delivery (Paul & Ellis Weismer, 2013).

**119.073 73** Early Identification of Autism Spectrum Disorder: Speech Language Pathologists' Knowledge, Screening, and Referral Practices. D. D. Barrie*, M. N. Gragg, K. Afridi and R. Jamil, *University of Windsor*

Background: Considerable evidence supports the feasibility of identifying children with Autism Spectrum Disorder (ASD) by 18 to 36 months of age. One of the most compelling reasons for early diagnosis is that it allows for intensive behavioural interventions early in life that could lead to more positive outcomes for children with ASD. Communication is one of the most common first concern of parents with children later diagnosed with ASD and parents often seek help or are referred to speech language pathologists (SLPs) for assessment and intervention for their children. SLPs working with very young children are in an opportune position to identify red flags pertaining to ASD early and to refer parents for formal assessment for early identification.

Objectives: To explore the knowledge, screening, and referral practices concerning ASD of Ontario speech language pathologists working with children under 6 years of age.

Methods: A sample of 199 speech language pathologists (years of experience: <5 years, *n* = 49; 5-9 years, *n* = 46; 10-15 years, *n* = 32; >15 years, *n* = 72) completed an on-line survey on their training, screening, and referral practices, the Autism Knowledge Survey-Revised (AKS-R), and demographic information. Comparison groups of 149 SLP graduate students, 167 undergraduate students and 16 specialists in the field of ASD also completed on-line surveys that included the Autism Knowledge Survey-Revised (AKS-R) and demographic information.

Results: Speech language pathologists' knowledge of ASD (as measured by the AKS-R) was significantly greater than that of SLP graduate students and undergraduate students. Eighty percent of SLPs agreed it was important to use formal screening tools when ASD was suspected compared to 97.3 % of SLP graduate students. Forty five percent of SLPs reported having the clinical expertise to identify most children with ASD without the use of a formal screening tool. When ASD was suspected, most SLPs reported rarely or never screening (67%), and almost always or always referring for formal assessment of ASD (64%).

Conclusions: Speech language pathologists are more likely to refer for formal assessment of ASD when suspecting that young children have ASD rather than formally screening for ASD. More SLPS believed in the importance of screening tools than used them. Most SLPs believed they can identify ASD in young children without screening tools. This emphasizes the importance of accessible and affordable training programs focusing on early signs and characteristics of ASD for speech language pathologists. Investigation of barriers to referral for formal assessment of ASD is also indicated. Data analysis is ongoing.

**119.074 74** Early Predictors of Parental Linguistic Mapping in Preschoolers with Autism Spectrum Disorders. B. Keceli Kaysili*[1], A. Tostanoski[2], L. R. Watson[3] and P. J. Yoder[2], (1)*Ankara University*, (2)*Vanderbilt University*, (3)*University of North Carolina*

Background: Parents may interpret children's frequent use of coordinated attention to communicative partner and referent (i.e. *triadic attention*) as an indicator that children will attend to, understand, and benefit from linguistic responses, which may in turn facilitate subsequent language development. Two types of triadic attention are (a) attention following and (b) intentional communication. One type of parental linguistic response occurs when parents "put into words" the presumed meaning of children's immediately preceding communication acts: *Parental linguistic mapping* (PLM). Frequency of PLM predicts later language in several populations of children with disabilities, including children with ASD. Identifying the predictors of PLM is one piece of evidence needed to identify pivotal skills for language development in children with ASD.

Objectives: Predictive relations were examined between (a) early frequency of intentional communication and attention following and (b) later frequency of PLM.

Methods: The study used a longitudinal correlational design (3 assessment periods conducted over 12 months). Although participants could get treatment, our project did not provide any during the study. Eighty-one minimally verbal preschoolers (age *M* = 35.2 months, *SD*= 7; mental age *M* = 12.3 months, *SD* = 5) participated in the current study. All children received a clinical diagnosis of autism (95.1%) or PDD-NOS (4.9%) from a licensed psychologist who used gold standard instruments, clinical best judgment according to DSM-IV-TR criteria. The two triadic attention skills were measured at Times 1 and Time 2 (4 months from Time 1) using the *Communication and Symbolic Behavior Scale*, *Early Social Communication Scales* and responsive examiner-child language samples. Frequency of PLM was measured at Time 2 and Time 3 (8 months from Time 2) using a semi-structured 10-minute parent-child snack session. Two multiple regression analyses using frequency of PLM at Time 2 as a control variable, one of the triadic attention skills as the predictor of interest, and frequency of PLM at Time 3 as the criterion variable were conducted.

Results: Initial frequency of PLM (partial r = .44) and early attention following (partial r = .27) predicted later frequency of PLM, $R^2$=0.29, p<0.01. Initial frequency of PLM (partial r = .45) and early intentional communication (partial r = .25) predicted later frequency of PLM, $R^2$=0.28, p<0.01.

Conclusions: The results are consistent with the hypothesis that the two triadic skills may encourage parents to use PLM. Identifying the predictors of PLM may sensitize parent trainers to the reasons some parents use more PLM than others. It is also possible that teaching parents to use another type of linguistic response (e.g., talking about children's focus of attention - follow-in utterances) might be a more adaptive parental skill during a period in which their children are not using triadic skills frequently. Indeed, past research in preschoolers with ASD found that PLM was predictive of later vocabulary only if children had a threshold level of comprehension (a probable correlate of triadic attention). Instead, follow-in utterances were predictive of language, even for the low-comprehension children (McDuffie & Yoder, 2010). More research is needed to address these possibilities.

**119.075 75** Generalisation of Word-Picture Relations in Children with Autism and Typically Developing Children. C. Hartley* and M. L. Allen, *Lancaster University*

Background:

Due to profound linguistic impairments, many low-functioning children with autism (CWA) are taught to communicate using pictorial symbols. Previous research has shown that CWA are significantly more likely to generalise labels to objects depicted in iconic colour pictures than non-colour pictures. However, it cannot be assumed that CWA privilege the same cues as typically developing children (TDC) when generalising words from colour pictures. From 2 years, TDC selectively generalise labels based on sameness of shape – the fundamental constraint underlying word-picture-object relations. By contrast, CWA often have difficulty categorising around the dimension of shape, and many fail to develop a 'shape bias' word learning heuristic.

Objectives:

Our objective was to identify whether CWA generalise labels from colour pictures based on similarity of shape, colour, or both shape and colour. We predicted that the absence of a shape bias may cause some CWA to over-extend labels to objects that match depicted referents on colour, but not shape.

Methods:

Seventeen CWA (*M* age = 9.7 years) were matched to 17 TDC (*M* age = 3.5 years) on receptive language (CWA: *M* = 3.5 years; TDC: *M* = 3.5 years). In each of 4 test trials, children were taught a novel word paired with a colour photograph of an unfamiliar target object, and then sorted a series of items into two containers according to whether or not they were a referent of the newly-learned label. Sorted items included 3-D target objects, differently-coloured variants of target objects, novel unfamiliar objects that were colour-matched to target objects, familiar objects, and pictures of each type of object.

Results:

CWA almost always extended labels to items that matched colour photographs on shape *and* colour (target picture: 100%; target object: 97.5%), but also frequently generalised to items that matched

only on shape (shape-match picture: 72.5%; shape-match object: 69%) *or* only on colour (colour-match picture: 69%; colour-match object: 61.8%). Two-thirds of CWA extended labels to shape-matched items and colour-matched items on 2-4 trials, suggesting their generalisation of word-picture relations was directed by both shape and colour. By contrast, TDC invariably generalised labels on the basis of shape (target picture: 100%; target object: 98.5%; shape-match picture: 100%; shape-match object: 98.5%), but rarely extended to items matching only on colour (colour-match picture: 11.8%; colour-match object: 7.3%). Neither group generalised words to familiar items.

Conclusions:

Low-functioning CWA understand that words paired with colour photographs can be extended to independently existing referents, however, they often generalise based on incorrect dimensions (i.e. colour). This atypical pattern of responding indicates a crucial misunderstanding of the rules that govern referential word-picture-object relations. Deficits in category formation may prevent CWA from privileging shape as a basis for generalising word-picture relations, meaning they are just as likely to extend words to items that match depicted objects on superficial perceptual details, such as colour. These findings have important implications for the design and delivery of picture-based communication interventions.

**119.076 76** Iconicity Influences How Effectively Children with Autism Use Pictures As Symbols in a Search Task. M. L. Allen* and C. Hartley, *Lancaster University*

Background:

In the absence of spoken language, many low-functioning children with autism (CWA) are taught to communicate using pictorial symbols. Previous studies examining the learning and generalisation of word-picture relations suggest that CWA may have difficulties understanding the symbolic nature of pictures. Here we investigate the ability of CWA to contextualise symbolic information communicated by pictures in a search task that did not involve word learning. Based on evidence from typically developing children (TDC), we anticipated that this ability may be influenced by iconicity (the extent that a picture resembles its referent) and/or access to linguistic representations corresponding to depicted referents.

Objectives:

Our objectives were a) to test whether CWA and TDC differ in their ability to contextualise pictures in a symbolic search task, and b) to identify whether their success is mediated by pictorial iconicity or access to labels for depicted referents.

Methods:

Sixteen CWA (*M* age = 9.9 years) were matched to 16 TDC (*M* age = 3.6 years) on receptive language (CWA: *M* = 3.6 years; TDC: *M* = 3.6 years). Children were introduced to a small toy character and a unique set of 4 occluders (various upturned buckets) that were individuated by familiar nameable objects or unfamiliar unnameable objects. The experimenter demonstrated the toy hiding underneath each occluder before presenting 4 pictures, one depicting each occluder. The experimenter highlighted the picture-referent correspondences and clearly asserted the intended purpose of the pictures. Out of the child's view, the toy was concealed underneath one of 4 occluders. Children were shown a picture of the hiding location and then searched for the toy. Over 3 sessions, children completed trials with 3 picture types – colour photographs, black-and-white line drawings and abstract colour pictures.

Results:

The results revealed zero group differences; neither CWA nor TDC were influenced by familiarity of depicted referents, and both groups' errorless retrieval rates (ERR) were above-chance with colour photographs (CWA ERR: 74%; TDC ERR: 81%), line drawings (CWA ERR: 58%; TDC ERR: 61%) and abstract pictures (CWA ERR: 62%; TDC ERR: 67%). However, both groups made significantly more errorless retrievals in the most-iconic photograph trials ($F = 12.93$, $p < .001$), and performance was universally predicted by receptive language. Children with relatively low receptive language (*M* = 2.9 years) only performed above-chance in photograph trials, while children with relatively high receptive language (*M* = 4.6 years) performed above-chance with all 3 picture types.

Conclusions:

In favourable experimental conditions, CWA can contextualise mental representations of pictures and use them to adaptively guide their behaviour. However, this ability is significantly influenced by iconicity and receptive language. The lack of a referent familiarity effect shows that CWA were not reliant on labelling depicted referents, suggesting that their linguistic development had a passive, yet critical, influence on their pictorial understanding. Overall, these results indicate that the picture comprehension difficulties experienced by CWA relate primarily to *word*-picture-object mapping, rather than picture-object mapping *per se*. Furthermore, our findings provide a data-ground rationale for delivering picture-based communication training with colour photographs.

**119.077 77** Joint Engagement and Social Communication in Minimally Verbal Children with ASD. A. Holbrook*[1] and C. Kasari[2], (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

Background: Both joint engagement and language have been studied in the context of parent-child dyads. It is well established that episodes of joint engagement facilitate children's early language development, but to our knowledge the relationship between joint engagement and social language between child and therapist is yet to be examined.

Objectives: This study examined the association between joint engagement and child language abilities within therapist-child interactions with minimally verbal children diagnosed with autism spectrum disorders.

Methods: Participants were selected from the large multi-site study, Characterizing Cognition in Nonverbal Individuals with ASD. All children used fewer than twenty spontaneous, functional words during a language sample, and had received at least two years of prior intervention. Videotaped baseline intervention sessions were coded for 61 children between the ages of 5 and 8 years. Episodes of joint engagement were defined as time a child and therapist coordinated their involvement around an object or activity. The mean length of joint engagement was used from the first intervention session. Child language abilities were: (1) total social communicative utterances (TSCU), which excluded all scripted utterances; (2) number of different word roots (NDWR), which represented the variety of novel words; (3) total number of comments (TCOM), defined as utterances used for the function of sharing information, or describing an action or object in their attentional focus. The language variables were averaged over the first two sessions to gain a more accurate representation of abilities from this minimally verbal population.

Results: The Spearman's rho revealed a statistically significant relationship between the mean length of joint engagement and TSCU ($r_s$ = 0.261, $p < 0.05$) and TCOM ($r_s$ = 0.309, $p< 0.05$). However, mean length of joint engagement was not significantly correlated with the NDWR.

Conclusions: Language abilities are a key target for minimally verbal children with autism spectrum disorders. Results demonstrate that joint engagement is associated with social communication and commenting language. Joint engagement between a child and a therapist may be a critical factor to facilitate social language development of minimally verbal children.

**119.078 78** Outcomes of Behavioral Intervention to Increase Single Word Requests to Multiword Requests in Children with Autism Spectrum Disorder. C. N. Bowen*[1], M. A. Shillingsburg[2] and R. Yosick[2], (1)*Marcus Autism Center*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*

Background: Children with ASD often require intervention for development of functional language (Eigsti, Marchena, Schuh, & Kelley, 2011). Initial intervention may focus on production of single-word requests; however, once single-word requests become consistent, interventions may aim to increase the mean length of utterance (MLU) the child uses. This is important since children with ASD often show delays in making the transition from single to multi-word speech. Paul, Chawarska, Klin, and Volkmar (2007) found that children with autism who had acquired nearly 100 single words in their vocabularies were not combining those words by the time typically developing children do. Thus, intervention to promote multi-word speech is warranted. Few published studies have examined interventions designed to increase the MLU, and most have relied on single-case research design and small samples. A review of the relevant research highlights the need for larger sample sizes and methods that aggregate single-subject data. Nonoverlap of All Pairs (NAP; Parker & Vannest, 2009) is a metric that allows for such aggregation of data from larger single-subject samples.

Objectives: The present study examines treatment outcomes of a behavior analytic intervention designed to increase the MLU in a larger sample of children with ASD (n=30). The NAP index (Parker & Vannest, 2009) was utilized to obtain an overall measure of intervention effectiveness (effect size).

Methods: Participants were identified via chart review. Inclusion criteria included: (a) attended intervention in an ABA-based language clinic and provided consent for dissemination of data (b) completion of at least five MLU treatment sessions. Of the 201 client charts searched, 30 clients met inclusion criteria. MLU treatment consisted of a therapist providing vocal prompts for lengthier requests. As MLU increased, requests of greater length were differentially reinforced. In order to quantify results across the sample, NAP was selected as a measure of intervention effectiveness. NAP was hand-calculated for each participant. The procedure outlined in Parker & Vannest (2009) for hand calculation of NAP was followed. All baseline datapoints were compared with all treatment datapoints and were divided by the total number of possible comparisons was calculated (number of baseline datapoints multiplied by number of treatment datapoints).

Results: Our sample consisted predominantly of males (80%) ages 2 to 13 years (mean 5.4 years) who were diagnosed with ASD (76.6%). Overall treatment effects were medium to large (average NAP=.89). Using NAP, the majority of the sample (70%) demonstrated strong treatment effects. The average *d* for the overall sample was 1.91, indicating a strong overall effect according to interpretive guidelines (Aberson, 2010).

Conclusions: The current study examined the effects of a behavior analytic treatment used to increase MLU in children with ASD in a sample of 30 single-case studies. Single-case data were successfully aggregated to produce a more comprehensive effect of the intervention to this population. Results suggest that targeted behavioral intervention to increase MLU was effective for the majority of participants in our sample.

**119.079 79** Peer Ratings of Videotaped Story-Telling of Optimal Outcome Children with a History of ASD. J. Suh*[1], I. M. Eigsti[1], L. Naigles[1], M. L. Barton[1], A. Orinstein[1], C. Irvine[1], D. T. Jashar[1], L. D. Haisley[1], E. A. Kelley[2] and D. A. Fein[1], (1)*University of Connecticut*, (2)*Queen's University*

Background: We are following children who have a history of autism spectrum disorder (ASD), who no longer meet diagnostic criteria for ASD. These children have achieved social and language skills within the average range, receive little or no school support, and are considered to have "optimal outcomes" (OO; Sutera et al., 2007; Helt et al., 2008; Kelley, Naigles, & Fein, 2010). However, it is unclear how *peers* perceive OO children.

Objectives: In a previous study, we asked naïve raters (aged 15-20) to rate *transcribed* narratives of stories told by children with OO, high-functioning autism (HFA), and typical development (TD) using the *Tuesday* book. Those results (reported at AACN 2013) indicated that OO and TD group stories did not differ, whereas HFA stories were harder to comprehend, contained more odd content, and were poorer in overall story quality. In the current study, high school peers rated *videos* of the narratives for "story goodness," pragmatic language qualities, and global presentation.

Methods: Forty-five participants with HFA, TD or OO (*n*=15 per group) completed the *Tuesday* story narration. Participants were matched on age (mean=12.9, range 9-15); while HFA group mean VIQ was slightly lower than the other two groups; no groups differed on NVIQ. Videos of the narrations were watched by five adolescents (ages 15-17), naïve to diagnosis, who rated the narratives on a five-point scale (1 = poor, 5 = excellent) for: overall story quality; dysfluency; ease of story comprehension; sophistication of language; correct use of grammar; presence of odd content and themes; and personal interest in the story. The students also rated the storyteller's overall "oddness."

Results: ANOVAs probed for group differences in peer story ratings. HFA ratings were significantly higher for *odd content and themes* [*M*(*SD*)= 3.9(0.7), 4.4(0.4), and 4.4(0.3) for HFA, OO, and TD, respectively; $p = .01$]; the OO and TD groups did not differ. The OO stories received marginally higher overall *quality* ratings than either TD or HFA [*M*(*SD*)= 3.0(0.3), 3.4(0.6), and 3.0(0.5) for HFA, OO, and TD, respectively; $p = .05$]. For overall *oddness*, OO and TD participants did not differ, and were rated as *less odd* than HFA participants [*M*(*SD*)= 3.4(0.7), 4.2(0.4), and

4.0(0.6) for HFA, OO, and TD, respectively; $p < .01$].

Conclusions: HFA narratives were rated as having more odd content than OO and TD narratives; there were *no* areas where peers rated OO narratives as poorer than TD narratives. Contrary to prior findings using transcribed narrative texts (Suh et al., 2013), videos of OO stories were rated *better* in *overall quality* than TD. It is possible that the story delivery (including vocal tone and gestures) made the OO stories more engaging. Finally, the HFA group was rated as generally more odd that the OO and TD groups; there was no difference between OO and TD children. Therefore, OO children produce stories equal to or better than those of TD children, suggesting significant symptom remission in the important domain of pragmatic language skills, as perceived by peers.

**119.080 80** Pretend Play As a Predictor of Expressive and Receptive Communication Skills in Preschool Aged Children: The Relative Contributions of Functional Versus Symbolic Play and Shared Versus Solitary Play. M. L. Fulton*[1] and B. D'Entremont[2], (1)*The University of New Brunswick*, (2)*University of New Brunswick*

Background: Pretend play has been found to be correlated with language development in both typically developing (TD) children and children with Autism Spectrum Disorder (ASD), although children with ASD exhibit less play (McCune-Nicolich, 1981; McCune, 1995, Mundy, et al., 1987). However, the more complex relationship between different types of pretend play (functional and symbolic) and expressive and receptive language is not well understood in children with ASD. Symbolic pretend play in particular has been theorized to have a predictive relationship with expressive language development in children as both require a similar form of symbolic understanding that is not required in functional pretend play (Lewis et al., 2000; Toth et al., 2006). There is also limited research testing whether symbolic pretend play is more predictive of expressive and receptive language than functional play for children with ASD. Finally, although pretend play is often social in nature, there is a paucity of research examining pretend play that is shared compared to solitary.

Objectives: To examine the ability of functional pretend play and symbolic pretend play to predict expressive and receptive language and explore differences in the relationship between shared versus solitary pretend play and language in children with and without ASD.

Methods: Data was collected from 11 children with ASD (*M*age = 60.18 months) and 11 TD children (*M*age = 40.45 months) matched on cognitive ability. Measures included the Autism Diagnostic Observation Schedule (ADOS), Psycho-Educational Profile- 3rd Edition, Preschool Language Scale- 4thEdition, and the Play Assessment Scale (PAS).

Results: Together, functional and symbolic pretend play predicted an additional 8% of the variance in expressive language, over and above cognitive ability and diagnosis ($F_{(2,16)} = 4.94$; $p = .02$). Only cognitive ability ($\beta = .43$, $p = .00$) and symbolic pretend play ($\beta = .41$, $p = .02$) contributed significantly to the final model. Functional pretend play did not contribute significantly to variance in expressive language. Within symbolic pretend play, solitary and shared play predicted an additional 7% of the variance in expressive language, over and above cognitive ability and diagnosis ($F_{(4,15)} = 4.57$, $p = .00$). Only cognitive ability ($\beta = .43$, $p = .00$) and shared pretend play ($\beta = .37$, $p = .02$) contributed significantly to the final model. Neither functional versus symbolic pretend play nor shared versus solitary pretend play predicted receptive language over and above cognition and diagnosis.

Conclusions: Results indicate that symbolic pretend play, particularly play that is shared, is related to expressive language but not to receptive language when controlling for cognition and diagnosis in children with ASD and TD children. These results support the theoretical link between symbolic pretend play and expressive language (Stanley, & Konstananreas, 2007).

In addition, the results suggest that play that is shared may provide opportunities for expressive language that are not present in solitary play. Further research could explore longitudinal relationships to determine whether increases in symbolic pretend play (particularly shared play) lead to increases in expressive language for children with ASD and for TD children.

**119.081 81** Prosodic Marking of Given, New, and Contrastive Information: Differences Between Children with and without ASD. J. E. Arnold*[1], E. C. Rosa[1], M. R. Klinger[2], P. S. Powell[2] and A. T. Meyer[3], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina - Chapel Hill*, (3)*University of North Carolina*

Background: Autism spectrum disorder (ASD) is characterized by deficits in communication, frequently involving impairment in prosody. One prosodic function is to mark information status, where stressed/prominent pronunciations are used for New or Contrastive information, while reduced pronunciations are used for Given (previously-mentioned) information. These patterns may stem from multiple cognitive mechanisms: 1) Application of a pragmatic rule about the conditions for prominent vs. reduced pronunciations. 2) Given words are easier to produce than New words, supporting fluent, reduced pronunciations. 3) Speakers may choose pronunciations to facilitate comprehension for the addressee. These mechanisms are not mutually exclusive, raising questions about which are impaired or spared in ASD.

Objectives: Better characterize the prosodic deficits associated with ASD, focusing on the information-status function of prosody. Identify mechanisms underlying prosodic production in children with and without ASD.

Methods: Children played a computer game with an experimenter. Both viewed a picture of four objects and four shapes per trial on their own computers (e.g., penny, tiger, doorknob, grapes, triangle, circle, square, star). The experimenter asked one of the following questions, and the child answered, e.g. "No, the tiger goes below the grapes." The target (the tiger) and its movement were indicated by an arrow on the child's screen.

(1) Given target: Does the tiger go below the triangle?

(2) New target: Does the penny go below the grapes?

(3) Contrastive target: Do the tiger and the doorknob go below the grapes?

Two blind coders rated the acoustic prominence of the target word pronunciation on a six-point scale (1=reduced; 6= prominent/emphatic). We predicted higher ratings in the New than Given conditions. This is the simplest pragmatic distinction. The Contrastive condition is important because it should elicit prosodic prominence through mechanisms (1) or (3) above. However, it involves the recent mention of the target word, which facilitates pronunciation, and by (2) is predicted to lead to reduction.

Additionally, we tested the child's sensitivity to the comprehension needs of the listener with a clarification filler half-way through the experiment ("Did you say dog or dock?") We compared pronunciations before and after this question as a measure of their response to the needs of the addressee.

Results: Preliminary results (18 ASD, 16 typically-developing (TD) participants) reveal that both groups produced similar greater prosodic prominence when the target was New than when it was Given. Both groups also responded similarly to the clarification filler, producing more prominent pronunciations after the clarification than before (for both Given and New targets). However, the groups responded differently to the Contrastive condition: for TD participants, the Contrastive condition was as prominent as the New condition, but for ASD participants, it was less reduced, similar to the Given condition.

Conclusions: The information-status function of prosody was largely preserved in a group of high-functioning children with ASD. However, using prosody to mark contrast was impaired. This reduced prominence for the Contrastive condition in the ASD group may reflect either a lack of pragmatic rule understanding, or a reliance on production facilitation over the addressee's needs.

**119.082 82** Self-Perception in Friendship Nomination in Children with Autism. B. L. Williams*[1], C. Kasari[2] and W. Shih[1], (1)*UCLA*, (2)*University of California Los Angeles*

**Background:**

Children with autism spectrum disorders (ASD) present with difficulty in establishing friendships. These difficulties become pronounced at school when children try to engage in age-appropriate social relationships, but lack the social and pragmatic skills to do so. As such, they report more loneliness than their neurotypical peers (Bauminger & Kasari, 2000). Because loneliness indicates a children's desire for relationships, it

may be that their desire and self-perception of friends begins early. This study examined child nominations of friendships in their school setting; both nominations of friends, and receipt of nominations from other children. It was hypothesized that children with greater discrepancy between desired friends (nominated and received) would show the least engagement in actual interactions with other children. Research on the relationship between self-perception and peer engagement is warranted to discover the impediments children with autism face developing friendships in school.

**Objectives:**

Objectives are to analyze if children with autism with more awareness of potential social connections with peers in school are more socially engaged in play settings than children with autism with less awareness.

**Methods:**

Participants in this study include 119 elementary school children with a diagnosis of autism in general education classrooms in grades K-5. Children completed a social network and friendship survey (Cairns and Cairns, 1994; Farmer and Farmer, 1996) that generated quantitative data on friendship groups and clusters in their school classrooms. The social network surveys yielded information on social awareness by analyzing the number of "out-degrees," nominated classroom peers identified as "friends" by children with ASD, and "in-degrees," nominations of the child with ASD identified as a "friend" by typical peers. Direct observation was collected by a reliable coder using the Playground Observation of Peer Engagement (POPE; Kasari et al., 2005) to assess peer engagement during lunch and recess by a blind rater. Data were analyzed from entry level measures at baseline and do not reflect treatment effects.

**Results:**

Analyses revealed a significantly positive Spearman correlation ($r = .22$, $p = .015$) between the number of out-degrees and high level peer engagement (games with rules or joint engagement) on the playground. Similarly, a significantly positive Spearman correlation ($r = .22$, $p = .015$) was found between children with autism with more in-degrees, or typical peer friendship nominations, and playground engagement.

**Conclusions:**

Children with autism who nominated more classroom peers as "friends" on their social network survey were more engaged on the playground in direct observation than children with autism who nominated fewer "friends." Likewise, children with autism who were more frequently nominated by their typical peers were also more engaged in play. These findings indicate that more awareness of peers as friends may translate to more social interaction attempts during lunch and recess. Further research is warranted on the barriers to developing friendships for children with ASD.

**119.083 83** Specific Language Impairment As Autism Endophenotype: A Meta-Analysis of Infant Sibling Studies. N. Marrus*[1], L. Hall[2], S. J. Paterson[3], J. T. Elison[4], J. J. Wolff[5], J. R. Pruett[1], H. C. Hazlett[5], A. M. Estes[6], J. Piven[5], K. N. Botteron[1], .. The IBIS Network[7] and J. N. Constantino[1], (1)*Washington University School of Medicine*, (2)*St. Louis Children's Hospital*, (3)*The Children's Hospital of Philadelphia*, (4)*University of Minnesota*, (5)*University of North Carolina at Chapel Hill*, (6)*University of Washington*, (7)*Autism Center of Excellence*

Background: The characterization of language impairments in the siblings of children with autism has considerable implications for understanding the genetic transmission of autism spectrum disorder (ASD), as well as the relationship between social cognition and language development. Previously, we observed the co-occurrence of language delay and subclinical autistic social impairments in a large sample of undiagnosed siblings of individuals with autism.

Objectives: To clarify the evidence that early language impairment, with or without accompanying social impairments, constitutes an autism endophenotype.

Methods: A meta-analysis was performed incorporating the scientific literature and unpublished data from the Infant Brain Imaging Study (IBIS), an ongoing multi-site study tracking brain and behavioral development in siblings of children with ASD and a low-risk control group. Seventy-four articles were identified via a search using the keywords "autism," "language," and

"sibling" for studies published in the PubMed database during the previous 10 years. Seventeen satisfied the following inclusion criteria: 1) implementation of standardized assessments of language and/or ASD, 2) inclusion of siblings of children with ASD (sibs-ASD) and typically developing children (TD), and 3) language data for both sibs-ASD and TD. A meta-analysis was performed incorporating the 7 published studies involving independent participants under 36 months (range 12-27 months) and data from IBIS. Among these 8 studies, 5 categorically identified subjects with and without language impairment (sibs-ASD: n=364, TD: n=228) while 5 reported expressive and receptive language scores from the Mullen Scales of Early Learning (MSEL) (sibs-ASD: n=389; TD: n=222). The Mantel-Haenszel (MH) method was used for dichotomous data and a random effects model with inverse variance weighting was used for continuous data. In the IBIS sample, the relationship between social motivation, as indexed by a subset of items from the Autism Observation Schedule for Infants (AOSI) at 12 months, and MSEL language scores was explored using a partial correlation controlling for the MSEL Early Learning Composite.

Results: The MH statistic indicated increased language impairment in sibs-ASD ($\chi^2_{MH}$=4.36, 1 d.f., p=0.037). Both receptive and expressive language scores showed positive effect sizes when comparing TD to sibs-ASD, signifying lower language scores in sibs-ASD. The summary effect size was moderate for receptive language, 0.540 (95% confidence interval: 0.450-0.630), and small for expressive language, 0.210 (95% confidence interval: 0.0043-0.416). None of the published studies examined correlations between language and social impairment. In IBIS, a significant correlation was observed for receptive language and social motivation items on the AOSI (r=-0.200, p=0.016), demonstrating an association of greater receptive language with decreased social deficits.

Conclusions: There is a dearth of studies characterizing language phenotypes in sibs-ASD. Current data support that language impairment comprises an endophenotype for ASD during early childhood. Receptive language appears more affected than expressive language, similar to previous reports of ASD populations, although the effect on expressive language may be independent of social function. More detailed characterization of this language impairment is needed to refine genetic investigations of ASD and our understanding of factors influencing the developmental progression of autistic traits.

**119.084 84** TITLE MISSING. S. L. Jordan*[1], L. H. Hampton[1], A. P. Kaiser[1] and C. Kasari[2], (1)*Vanderbilt University*, (2)*University of California Los Angeles*

Background: There is a critical need for effective interventions for children with ASD who remain nonverbal after the age of 5 (Kasari, Tager-Flusberg et al, 2013). The development of an innovative naturalistic intervention, JASP-EMT was examined in a randomized trial (Kasari et al, submitted). An important variation in this trial was the addition of Augmentative and Alternative Communication (AAC) has to determine if adding an augmented mode could increase expressive language for children that are minimally verbal (Olive et al., 2006).

Objectives: This current study examined the use of Augmentative and Alternative Communication (AAC) and spoken langauge with a subset of minimally verbal children with Autism who participated in a randomized trial JASP-EMT. Specifically, this study examined the effects that JASP-EMT had with AAC use on spoken and AAC generated spontaneous social communication (SCU) during the course of the intervention as well compared results before and after intervention. The following questions were addressed in this study: 1. What are the effects of JASP-EMT with AAC on spoken social communication? What are the effects on AAC use? 3. What is the relationship of AAC and spoken language use?

Methods: The participants in this study included 20 minimally verbal children with ASD ( less than 20 unique words) from the one site of the RTC. Children were on average 6.48 years old (SD=1.11) with a mean IQ of 63.43 (SD=22.9). Ten participants were randomly assigned to JASPER-EMT plus AAC and 10 were assigned to JASPER-EMT without AAC. In the first phase of intervention, participants received two 45 minute sessions/ week of JASP-EMT for 12 weeks. The two conditions differed only in the inclusion of the AAC device. Interventionists modeled target level language on the AAC device 50% of all utterances, and expanded child utterances on the AAC device 50% of all expansions. A 10-minute

video sample was transcribed and coded from 25% (total 6) of intervention sessions. Spoken socially communicative utterances (SCU) and AAC use were measured in each session. In addition, SCU and AAC were measured at the pre and post intervention sessions

Results: Children in the AAC condition produced more socially communicative utterances (M=19.2, SD=29.3) at the end of intervention than children in the spoken language intervention only (M=5.5, SD=42.8, d=.373). As participants in the AAC condition increased their verbal social communication, AAC use decreased. On average, participants initiated only 2 AAC utterances per session (SD=1.06), however, they used more spoken language than children in the spoken language condition only. Additional analysis will examine the sequential relationship between therapist use of AAC and child use of AAC and spoken language, and how the child responded when the adult activated the AAC.

Conclusions: Minimally verbal children with Autism demonstrated greater gains in spoken social communication during a naturalistic intervention including AAC. AAC use did not maintain once children learned to use verbal communication. Further research is required to understand if adult AAC models and generalized use of AAC across routines can help to increase number of different words (NDW).

**119.085 85** The Impact of Birth Order and Sibling Age on Language in Individuals with ASD. A. Kresse*, E. J. Libsack, T. Ward, K. Ankenman, E. E. Neuhaus, S. Faja, S. J. Webb and R. Bernier, *University of Washington*

Background:

Impaired communication is one of the core features of autism. In typical development, siblings can positively influence language development and outcomes (e.g., Hoff-Ginsberg, 1998, Bernicot & Roux, 1998) though birth order plays a role in the nature and size of these effects. Although children with ASD participate in fewer prosocial interactions with their siblings compared to children with down syndrome (Knott et al., 2007) the presence of a sibling in the home may still impact their development. Siblings provide in-home opportunities for practice socializing with peers, but they also introduce competition for parent attention.

Objectives:

This study combines data collected from the University of Washington Twin Study and the Simons Simplex Collection to explore the impact of a typically developing sibling on language and communication in individuals with autism.

Methods:

First, we matched the ASD affected individual (e.g., proband) from 14 disconcordant twin pairs and 37 disconcordant sibling pairs on age and gender. Probands were between 4 and 17 years (M = 10.3, SD = 3.23). Next, groups were divided based on the age difference between the proband and sibling: (1) proband younger than TD sib by ≥2.5 years (N = 16); (2) probands younger than TD sib by <2.5 years (N = 18); (3) twins (N = 14); (4) proband older than TD sib <2.5 years (N = 21); (5) probands older than TD sib by ≥2.5 years (N = 14). Analyses included scores from the ADOS, ADI, IQ and Vineland for the proband and Vineland for the Sib.

Results:

ASD individuals with a twin or a younger sibling have marginally higher verbal IQ scores compared to ASD individuals with an older sibling (<2.5 years) (ps < .08). Probands with a much older sibling (≥2.5 years) have significantly better communication scores on the ADOS compared to those with a sibling <2.5 years older (p = .002) and marginally better scores than those with a sibling <2.5 years younger (p = .09). ASD individuals with a much younger sibling (≥2.5 years) have significantly better ADOS communication scores than those with a sibling <2.5 years younger (p = .02).

Conclusions:

Children with ASD who have a twin or younger sibling have higher verbal IQ compared to those with older siblings. For communication scores on the ADOS (which includes items such as stereotyped language and conversation skills), individuals with ASD who were most dissimilar in age to their sib were less impaired than those whose sibling was closer to their own age. Taken together, these findings suggest that birth order and sibling spacing in "simplex" families impact social and communication abilities in children with

ASD. Analyses will also be presented on adaptive skills in the probands and sibling.

**119.086 86** The Influence of Semantic Richness on Novel Word Learning in Children with Autism Spectrum Disorder. A. Gladfelter* and L. Goffman, *Purdue University*

Background: The development of words (Howlin, 2003) is delayed in children with autism spectrum disorder (ASD). These children often continue to lag behind their peers in their vocabulary growth into their school years, and almost 20% remain functionally nonverbal (Lord et al., 2004). When children with typical language development (TLD) first map a novel word form with meaning, they benefit from learning words in rich semantic contexts (McGregor et al., 2007). Further, their speech motor stability increases when novel word forms are taught with visual referents (Heisler, Goffman, & Younger, 2010). Motor deficits (Bhat et al., 2012; Landa et al., 2013; Liu & Breslin, 2013) and vocal stereotypies (Rapp et al., 2013) are well documented in children with ASD. However, little is known about how their articulatory systems change across the timecourse of word learning, especially as a function of semantic knowledge.

Objectives: The inclusion of semantic cues enhances semantic, phonological, and articulatory performance on word learning tasks in children with TLD (Gladfelter & Goffman, 2013; Heisler et al., 2010; Storkel & Adlof, 2009). The goal of our study was to investigate whether and how comprehension and production of words and phonetic accuracy and articulatory variability are influenced by semantic cues in children with ASD.

Methods: Twelve children with ASD and 12 children with TLD (matched for expressive vocabulary level, all typical nonverbal IQ) were taught six novel words across three experimental sessions. The words were divided into three semantic learning conditions: no semantic cues, sparse semantic cues (visual referent only), and rich semantic cues (a story including multiple attributes of the word). Traditional measures of learning included: comprehension and production probes and a definition task. Phonetic transcriptions of imitated productions during the pre- and post-tests were analyzed to compare phonetic accuracy before and after learning the novel words. Articulatory movement recordings were collected from the upper and lower lip and jaw and analyses of speech motor variability (e.g., Gladfelter & Goffman, 2013) were conducted both in the pre- and the post-tests. Critical comparisons were whether semantic cues facilitated word learning in children with ASD and TLD.

Results: Both children with ASD and their TLD peers improved their performance on comprehension, production, and definition tasks as semantic richness increased. Children with ASD were even more responsive than their peers to the highly informative cues in the rich story condition, and this benefit was observed from the onset of the first session and maintained across sessions. Articulatory measures were especially sensitive to the depth of semantic context, with the children with ASD only improving in movement stability for the words taught with the rich semantic cues included in the story condition. Children with TLD also benefitted from semantic cues, but responded similarly in the sparse (visual referent) and the rich (story) contexts.

Conclusions: Measures of knowledge, sound accuracy, and articulatory movement stability all converge to reveal that children with ASD, even more than their TLD peers, benefit from exposure to rich semantic contexts during their earliest acquisition of new words.

**119.087 87** The Relation Between Pragmatic Language Impairment and Bully Victimization in Children with ASD. P. Rao* and R. Landa, *Kennedy Krieger Institute*

**Background:** The CDC has declared "bullying among youth to be a significant public health problem." According to a recent national longitudinal study, 24.5% of children are victims of bullying during elementary school; prevalence rates increase to 34.1% during middle school. Children with ASD experience rates of bully victimization 16 times that of typically developing children. While there is a general consensus that communication problems are related to peer relational difficulties, to date, little is known about what aspects of communication are related to heightened vulnerability to bully victimization in children with ASD.

**Objectives:** The purpose of the present study was to investigate the relation between pragmatic language impairment and bully victimization. Pragmatic language impairment involves a mismatch between communication behavior and social context. We hypothesized that pragmatic

language impairment would be associated with bully victimization, above and beyond verbal IQ and general communication abilities, because, unlike these aspects of functioning, pragmatics is impaired in all individuals with ASD, regardless of verbal or nonverbal cognitive functioning.

**Methods:** 44 children (ages 9 - 13 years) participating in a longitudinal study of development in children at high and low risk for ASD. Children were classified as: ASD (n = 21) and Non-ASD (n = 23); mean age = 10.00; SD = 1.13. Bully Victimization was measured with the Victimization T-score from the *Reynolds Bullying Victimization Scales for Schools* (RBVSS). Pragmatic Language Impairment and General Communication were assessed with the Social Interaction Deviance Index (SIDI) and the General Communication Composite (GCC) score of the *Children's Communication Checklist-2* (CCC-2). Verbal IQ was measured using the VIQ standard score of the *Stanford-Binet Intelligence Scales, Fifth edition* (SB-5).

**Results:** Chi-Square analyses revealed that a significantly higher percentage of children with ASD scored in the clinically significant range on the Victimization subscale of the RBVSS than children without ASD (42.9% versus 0%, respectively; $X^2$ = 12.39, Fisher's = .0001). Mann-Whitney nonparametric tests revealed that children with ASD scored significantly lower in verbal IQ ($Z$ = -4.16, $p$ = .0001), and significantly more impaired in pragmatic language ($Z$ = -2.75, $p$ = .006) and general communication ($Z$ = -3.69, $p$= .0001) than children without ASD.

To test our hypothesis that pragmatic language impairment would be associated with bully victimization, above and beyond verbal IQ and general communication, we conducted a linear multiple regression analysis with standard scores from the VIQ, GCC and SIDI as independent variables, and the Victimization T-score from the RBVSS as the criterion variable. As hypothesized, the SIDI pragmatic language impairment score significantly predicted Bully Victimization (F = 5.00; p = .03), explaining14% of the variance (R = .36). The other IVs were excluded from the model in the linear regression.

**Conclusions:** The results of this study supported our hypothesis. Pragmatic language impairment, over and above lower verbal IQ and general communication, is significantly related to bully victimization in children with ASD. The impact of early and ongoing pragmatic language intervention on bully victimization of children with ASD should be examined.

**119.088 88** The Relation Between Teacher Functional Communication and Anxiety in Children with ASD. E. F. Geib*[1], J. Berg[2], H. N. Davis[2], B. J. Wilson[2] and C. L. Teel[2], (1)*Clinical Psychology, Seattle Pacific University*, (2)*Seattle Pacific University*

Background:

Researchers report significantly elevated rates of anxiety disorders in children with autism spectrum disorders (ASD) (Lopata et al., 2010; White, Oswald, Ollendick, & Scahill, 2009). This trend suggests the need for future anxiety focused interventions and exploration of this phenomenon in early development. Recently, studies have focused on the association between anxiety and adolescence in individuals with high functioning autism (Bellini, 2004; Myles et al., 2001; White et al., 2010). Co-morbid anxiety has also been associated with elevated social language impairments (Bellini, 2004; Myles et al., 2001). A further analysis of the relation between anxiety and functional communication skills in younger children will expand knowledge of anxiety development in children with ASD.

Objectives:

The purpose of our study was to assess the relation between functional communication skills and anxiety symptomology in children with ASD and children with typical development (TD).

Methods:

Our preliminary sample included 86 children ages 3:1 to 6:11 and their teachers. Fifty-five children (45% female; 55% male) were typically developing and thirty-one children were diagnosed with ASD (16% female; 84% male). Teachers completed questionnaires assessing children's functional commination and anxiety symptoms (BASC, 2nd edition). Data collection for this study is ongoing.

Results:

A hierarchical regression analysis was used to examine the influence of developmental status and functional communication skills on anxiety

symptoms. Child age and verbal ability were entered in the first step as control variables and did not predict significant variance, $R^2$ = .026, $F(2, 83) = 2.23$, $p$ = .974. Developmental status entered on the second step also did not contribute significant variance to anxiety symptoms, $\Delta R^2$ = .070, $F(2, 81) = 3.04$, $p$ = .053. In the final step of the regression analysis, the interaction term between developmental status and functional communication skills accounted for a significant proportion of the variance in child anxiety symptoms, $\Delta R^2$ = .051, $F(1, 80) = 4.67$, $p$ =.034. Children with ASD who were rated by teachers as having higher functional communication skills were reported to have significantly greater anxiety symptoms than children with lower functional communication skills. Typically developing children had similar levels of anxiety regardless of level of functional communication skills.

Conclusions:

Findings indicated children with ASD with the highest levels of functional communication skills received the highest ratings of anxiety symptomology per teacher report. Children with greater functional communication skills may be better able to communicate their distress leading caregivers and teachers to perceive higher anxiety. In addition, functional communication skills may correlate with other factors such as intelligence and awareness of deficits that make children with ASD more likely to experience anxiety symptoms. Functional communication skills may serve as a strength that can be utilized during interventions targeting anxiety in children with ASD.

**119.089 89** The Role of Social Language in the Student Teacher Relationship. M. Maye*[1], M. Feldman[1], A. Eisenhower[1] and J. Blacher[2], (1)*University of Massachusetts, Boston*, (2)*University of California - Riverside*

Background: Little is known regarding the factors that affect student-teacher relationship (STR) quality in children with Autism Spectrum Disorder (ASD). However, positive STRs have been demonstrated to be important predictors of social, academic and behavioral outcomes in typical-developing populations (Hamre & Pianta, 2001). Few studies have examined STRs among children with ASD; two such studies have found that STR quality is predicted by behavioral difficulties (Brown & McIntosh, 2012; Robertson, Chamberlain, & Kasari, 2003). However, no known studies have examined the association between social communication and STR quality among children with ASD, despite the fact that social communication deficits are core symptoms of ASD. The current study is aimed at examining how aspects of social communication, specifically language factors, predict STR quality among young children with ASD during the early school years. Understanding the impact of social language factors on STR quality for children with ASD is imperative given the demonstrated importance of STRs in terms of future social, academic, and behavioral success.

Objectives: 1. Identify associations between global and social language factors and STR quality among children with ASD during the early school years. 2. Examine how teacher and classroom factors (professional training, type of classroom) moderate the association between language and STR quality.

Methods: Participants were evaluated three times across 1.5 years as part of a longitudinal, multi-method study of the adaptation to school among children with ASD. The current sample includes 123 participants who were entering pre-K, kindergarten, or first grade at the time of enrollment; all had confirmed ASD diagnoses according to the Autism Diagnostic Observation Schedule (ADOS) and clinical impression. Ninety percent of participants were receiving special education services in school. Enrollment is ongoing; approximately 60 additional participants will be added by April of 2014. Language was assessed with performance-based (ADOS and Comprehensive Assessment of Spoken Language; CASL) and parent-reported (Children's Communication Checklist; CCC-2) measures; STR quality was evaluated with the teacher-reported Student-Teacher Relationship Scale.

Results: Missingness will be addressed using full information maximum likelihood. Subscales related to global language competencies [syntax: $F(1,94)=9.79$, $p<.01$, $R^2=.09$, basic concepts: $F(82,1)=9.17$, $p<.01$, $R^2=.10$] ], as well as, social language factors [pragmatic language: $F(1,93)=11.76$, $p<.01$, $R^2=.11$], significantly predicted overall STR quality. ADOS item-level scores of immediate echolalia [$F(1,94)=5.74$, $p=.02$, $R^2=.06$] and conversational skills [$F(1,93)=5.54$, $p=.02$, $R^2=.06$] also predicted STR quality. No significant relationships were observed

between remaining ADOS communication items nor CCC-2 subscales and overall STR. Subsequent analyses will examine potential moderating effects of teacher and classroom factors.

Conclusions: Significant associations were observed between language skills and STR quality among young children with ASD; our findings suggest that, in addition to overall spoken language skills, children's pragmatic language abilities as well as their ASD-specific speech patterns (echolalia) were important to their STRs. Given the documented importance of the STR on children's long-term academic, social, and behavioral trajectories, such research may aid in identifying predictors of STR that may be specific to ASD and may inform interventions aimed at improved academic outcomes.

**119.090 90** The Role of Supported Joint Engagement and Parent Utterances in Language and Social Communication Development in Children with ASD. K. M. Bottema-Beutel*[1], P. J. Yoder[2] and L. R. Watson[3], (1)*Lynch School of Education, Boston College*, (2)*Vanderbilt University*, (3)*University of North Carolina*

Background:

In young children with autism spectrum disorder (ASD), social communication and language abilities in early childhood impact adult social functioning, independence, and adaptive behavior (Gillespie-Lynch, Sepeta, & Wang et al., 2012). Many of these children do not develop language (Klinger, Dawson, & Renner, 2002), and are at risk for poor adult outcomes. Social communication difficulties are endemic to ASD, and persist through adulthood regardless of language abilities (Tager-Flusberg, Joseph, & Folstein, 2001). Previous research has shown early parent-child interactions play an important role in language and social communication development. Supported joint engagement (SJE), in which the parent scaffolds play so that the child is not required to manage the interaction through eye contact, predicts later expressive and receptive language in children with ASD (Adamson et al., 2009). Additionally, parent utterances that follow the child's focus of attention also predict expressive language, receptive language, and social communication (McDuffie & Yoder, 2010; Siller & Sigman, 2002). In this study, we extend this literature by dividing SJE into higher order (HSJE) and lower order (LSJE) variants, with HSJE involving some degree of reciprocity from the child. We also examined follow-in utterances that co-occurred with object engagement, HSJE and LSJE.

Objectives: 1) To determine if HSJE is the superior predictor of expressive language, receptive language, and social communication, as compared to LSJE or object engagement, 2) To determine if follow-in utterances that co-occur with HSJE predict language and social communication to a greater extent than follow-in utterances that co-occur with LSJE or object engagement.

Methods: At time one, seventy-nine initially nonverbal preschoolers ASD were administered a video recorded parent- child interaction procedure and were assessed for mental age. Eight months later, participants were assessed for expressive language, receptive language, and social communication. Videos were coded for engagement states and parent follow-in utterances. Multiple linear regressions were used to determine significant predictors for each outcome.

Results: Only HSJE predicted social communication and expressive language, while object engagement and mental age predicted receptive language. In a separate set of regressions that include each engagement state combined with follow-in utterances, HSJE combined with follow-in utterances and mental age predicted all three outcomes. In three final regression models that included the total proportion of HSJE and HSJE combined with follow in utterances, only HSJE combined with follow-in utterances predicted receptive language, while only the total proportion of HSJE predicted expressive language and social communication.

Conclusions: Supported joint engagement can be meaningfully separated into HSJE and LSJE, and only HSJE predicts expressive language and social communication. The engagement framework during the provision of follow-in utterances is also important, with the HSJE framework solely predicting each outcome. Lastly, total HSJE has importance above and beyond follow-in utterances provided during this state for expressive language and social communication, highlighting the importance of scaffolded engagement that involves some degree of reciprocity from the child. Receptive language is influenced by follow-in

utterances provided during HSJE, even when controlling for total HSJE, highlighting the importance of optimal linguistic input for this outcome.

**119.091 91** Use and Misuse of Common Ground, a Complex Pragmatic Language Skill, in Adolescents with Autism Spectrum Disorder. A. de Marchena*[1] and I. M. Eigsti[2], (1)*The Children's Hospital of Philadelphia*, (2)*University of Connecticut*

**Background:** Pragmatic language is a complex, multi-faceted domain that includes such diverse skill sets as reciprocal conversational skills (e.g., turn-taking), word choice based on specific conversational partners (e.g., register), and the comprehension and use of nonverbal aspects of communication that complement speech. Deficits in pragmatic language are essentially universal in individuals with autism spectrum disorder (ASD) and are often reported to be a significant source of social anxiety for these individuals. While pragmatic language has been the focus of significant research in ASD, many aspects of this complex domain have yet to be investigated at all.

**Objectives:** In this study, we use an experimental narrative task to study a specific pragmatic language skill, *common ground*, and its use in adolescents with and without ASD. Common ground refers to the tendency of interlocutors to modify how they communicate based on shared knowledge. This skill has not been specifically investigated in an ASD sample to date.

**Methods:** Adolescents with ASD ($n$ = 18) and typical development (TD; $n$ = 18) were matched on chronological age, IQ, and receptive vocabulary. All participants had IQ scores in the average range. For the experimental task, participants told stories based on cartoon stimuli to a listener. The existence of common ground was experimentally manipulated such that participants told stories in one of two conditions: (A) the *private* condition, in which information about the cartoon was known only to the participant, thus the listener and participant had no common ground and (B) the *shared* condition, in which the listener and participant shared knowledge about the cartoon and thus had common ground. Three narratives were told in each condition, for a total of six narratives per participant. Story word count was the primary dependent measure.

**Results:** Consistent with prior research, TD participants produced reliably shorter narrations when they shared knowledge with an interlocutor, an effect not observed in participants with ASD (Group X Condition interaction: $F(1,34) = 5.31$, $p = .03$, partial $h^2 = 0.14$). This effect was unrelated to general skills such as IQ or receptive vocabulary. In the ASD group, the effect was correlated with age, and with symptom severity: younger and more severely affected participants showed little evidence of common ground, while older, more socially skilled participant appeared to demonstrate the skill. Qualitative data suggested that participants with ASD were attempting to use common ground, but were not consistently successful in doing so.

**Conclusions:** Adolescents with ASD were attempting to use common ground but had not yet developed the subtle, implicit approach of their TD peers. Results suggest essentially stable abilities for TD adolescents, while adolescents with ASD show delays, and emerging skills, in this important pragmatic domain. These findings highlight the need for continued intervention targeting discourse skills into adolescence, and suggest that adolescents with ASD may be particularly open to change in this domain.

**119.092 92** "Story Goodness" in Adolescents with Autism Spectrum Disorders. A. R. Canfield*[1], I. M. Eigsti[1] and A. de Marchena[2], (1)*University of Connecticut*, (2)*The Children's Hospital of Philadelphia*

Background: Individuals with autism spectrum disorders (ASD) have well-documented deficits in pragmatic language. Narrative elicitation is a particularly useful tool for examining pragmatic language, as it requires the speaker to provide and organize the relevant information to ensure the listener's comprehension. Prior studies of "story grammar," the organization of story components into logical relationships between characters and other story events, have proved it to be a quantitative measure of sociocommunicative abilities (e.g., in adults with brain injury; Coelho, 2002). Story grammar, along with story "completeness," seems to capture what naïve listeners perceive as story "goodness" (Le et al 2011).

Objectives: Our objective was to study narrative quality in ASD as a means of understanding the pragmatic language deficits associated with the disorder. We compared narratives produced by adolescents with typical development (TD) and ASD using the quantitative methods described above (i.e., story goodness and story grammar), and through the use of real-world listener comprehension measures.

Methods: Adolescents with ASD and TD ($n$= 15 per group) were matched on chronological age, gender, and full scale IQ. As part of the Autism Diagnostic Observation Schedule (ADOS), participants were shown a series of pictures of black and white drawings that depict a story about two monkeys. After these cards were removed, the adolescents were asked to tell the examiner the story from the pictures. These narratives were transcribed and broken into minimal grammatical units (T-units) for coding purposes. The narratives were evaluated for the proportion of T-units within story grammar structure, yielding a story grammar score, and the presence of six core events, yielding a story completeness score. Transcribed narrations were also rated by college students, naïve to diagnosis and study hypotheses, as a measure of story goodness, fidelity to the provided story, coherence, and oddness.

Results: Participants with ASD and TD did not differ on the measure of story grammar, indicating that narratives of both groups were similarly organized. While both groups produced a similar total number of T-units, the ASD group included significantly fewer core story events than the TD group $F(1, 28) = 4.093$, $p = 0.053$, partial $\eta^2 = 0.128$, such that stories were less complete. Undergraduate raters found the stories of the ASD group to be significantly less good overall ("how good a story is this?") than those of the TD group, $F(1, 28) = 15.829$, $p < 0.001$; however, stories did not differ by group for ratings of accuracy, coherence, and oddness. This indicates that the raters detected a global difference between the narratives of the two groups, but were unable to specify the fine-grained details of this global difference.

Conclusions: Adolescents with ASD produced similarly structured, yet less complete narratives than adolescents with TD. Untrained raters were sensitive to this global difference in the ASD group's narratives. As narratives are central in much of our daily communication, these findings suggest that this method of evaluating narratives may provide a sensitive measure of current sociocommunicative abilities and changes in response to intervention in adolescents with ASD.

## 120 Early Development

**120.093 93** Early ASD Symptom Severity Predicts Diagnostic Transition to Global Developmental Delay (GDD). D. N. Abrams*[1], D. Robins[1], L. B. Adamson[1] and D. A. Fein[2], (1)*Georgia State University*, (2)*University of Connecticut*

Background: Although early diagnosis of Autism Spectrum Disorders (ASD) is generally stable over time, some toddlers diagnosed with ASD no longer meet criteria when they are older. In particular, some initially diagnosed with ASD are later diagnosed instead with Global Developmental Delay (GDD). This may be due to difficulty distinguishing between these disorders at a young age, or due to change in symptom presentation over time. Studies have sought to identify initial differences between individuals with ASD and those with GDD. Results have been variable, though children with ASD tend to have greater impairment in social responsiveness and more restricted, repetitive, and stereotyped behaviors. Despite these group comparisons, research on predictors of diagnostic transition between these disorders is limited.

Objectives: To identify abilities and symptoms in toddlers with ASD at a 2-year-old evaluation which predict being diagnosed with GDD and no longer meeting ASD criteria by age 4.

Methods: 214 children (174 males, 81%) who had been diagnosed with ASD at age 2 (T1, $M$=26.44 months, $SD$=4.51) were re-evaluated near age 4 (T2, $M$=49.73 months, $SD$=6.85). The initial evaluation occurred after the child screened positive on the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 1999) or was flagged by a pediatrician for possible ASD. Evaluations included ADOS, Vineland Adaptive Behavior Scales (-II; VABS), and Mullen Scales of Early Learning (MSEL).

Results: Of the 214 toddlers given an ASD diagnosis at T1, 15 (7%) no longer met criteria for ASD at T2 and were diagnosed with GDD (ASD-GDD); 199 maintained their ASD diagnosis (ASD-ASD). Logistic regression revealed that although all children met criteria for ASD at T1, those with

lower ADOS comparison scores at T1 were more likely to meet criteria for GDD rather than ASD at T2, *OR*=.74, *p*=.02. Fewer DSM-IV-TR symptoms at T1 in the social domain also predicted transitioning from ASD to GDD diagnosis, *OR*=.30, *p*<.001. However, sex and measures of cognitive and language ability (MSEL, VABS) were not related to this diagnostic transition, *p*>.05.

Conclusions: Although all children met criteria for ASD at T1, toddlers who would later be diagnosed with GDD (ASD-GDD) had milder ASD symptom severity at T1 than the ASD-ASD group. These results indicate that those who change diagnosis from ASD to GDD over time may be differentiable from those with stable ASD at initial diagnosis. Furthermore, instability in the ASD-GDD group is due to differences in ASD symptom severity, and not by differences in cognitive and language ability. This has clinical implications for accurate early diagnosis of developmental disorders and their treatment. However, the lack of other group differences, such as in cognitive and language ability, contribute to the difficulty in differentiating between these disorders at a young age. Future research will examine the role of intervention in the diagnostic transition of these toddlers.

**120.094 94** ASD Symptoms in Unaffected Younger Siblings of Children with and without ASD: A Prospective Study. I. Giserman Kiss* and A. S. Carter, *University of Massachusetts Boston*

**Background:** Research following infants with an older sibling diagnosed with ASD has informed understanding of the early course of the disorder and has documented an infant sibling recurrence risk of 18.7% (Ozonoff et al., 2011). Prospective studies eliminate many limitations encountered in retrospective research, such as recall bias; prospective studies suggest that ASD symptoms emerge over the second half of the first year of life and beyond. There is a growing body of literature examining milder ASD symptoms present in relatives of individuals diagnosed with the disorder, frequently referred to as the broader autism phenotype (BAP). A recent study by Georgiades and colleagues (2013) suggested that 19% of unaffected siblings of children with ASD showed a BAP symptom profile at 12 months of age.

**Objectives:** This study investigates whether infant siblings of probands with ASD, who do not themselves meet diagnostic criteria for ASD at 24 or 36 months of age, are rated by parents as exhibiting more ASD symptoms at 12, 18, and 24 months than infants with typically developing siblings who also do not meet criteria for ASD.

**Methods:** Data are presented on 26 unaffected high risk (HR) younger siblings of probands (46.15% male), and 35 low risk (LR) control participants with typically developing siblings (45.71% male). Proband and infant sibling ASD diagnoses were made or ruled-out using gold-standard diagnostic measures and clinical judgment. All participants included in this report did not meet criteria for ASD or other developmental concerns (e.g., language delays). Parents of participants completed the Brief Infant-Toddler Social Emotional Assessment (BITSEA) at 12, 18, and 24 months of age. Analyses examine the ASD Problems subscale of the BITSEA, which consists of nine problem behaviors often present in young children diagnosed with ASD (e.g., Puts things in a special order over and over).

**Results:** A repeated measures ANOVA was used to assess mean differences on the BITSEA ASD Problems subscale between the HR and LR groups across 12, 18, and 24 months of age. Multivariate results revealed a significant reduction over time on BITSEA ASD Problems score.
Wilks' Lamba=.32, and this was statistically significant, ($F(2,58)=62.10$, $p<.001$). 68% of variance in BITSEA ASD Problems scores is accounted for by time ($\eta_p^2=.68$). The interaction between time and risk group was non-significant, indicating that the difference between groups did not vary across time. Tests of between-subjects effects showed a significant main effect of group membership ($F(1, 59)=4.94$, $p=.03$), with HR participants having higher mean scores than LR participants. Final analyses will include imputed missing values and data from infant siblings who receive a diagnosis of ASD.

**Conclusions:** These preliminary results are consistent with recent findings regarding the early emergence of BAP traits in unaffected siblings (Georgiades et al., 2013); unaffected infant siblings of probands displayed more ASD-relevant problem behaviors than infants with typically developing siblings. Findings support the importance of monitoring the emergence of ASD symptoms in younger siblings of children diagnosed with ASD through routine

developmental screening and surveillance as they may benefit from early intervention services.

**120.095 95** Context Matters: The Measure of Emotion Regulation in Autism. M. E. Crisler*[1], A. B. Barber[1], J. E. Lochman[1] and H. M. Swingle[2], (1)*University of Alabama*, (2)*University of South Alabama*

Background: Emotion regulation (ER) development in autism spectrum disorder (ASD) is not clearly documented, despite frequent reference across literature and assessment measures. ER is a reported difficulty in ASD, though is currently not a core target of intervention objectives (Mazefsky Pelphrey, & Dahl, 2012), which may be reflective of limited assessment tools that adequately capture ER skills across multiple contexts. The *modal model* theory presents the following steps in ER: 1) situation selection; 2) situation modification; 3) attention deployment; 4) cognitive change; 5) and response modulation (Gross & Thompson, 2007). The modal model provides a logical framework within which ER may be assessed in young children.

Objectives: Three research goals are examined: 1) the development of an observational measure based on the modal model of Gross & Thompson, the Emotion Regulation Assessment for Autism (ERAA); 2) the comparison of ERAA ratings across diagnostic groups; and 3) the examination of ER difficulties as they relate to ASD across different play contexts and partners.

Methods: Thirty-one children diagnosed with ASD and 31 children with typical development were recruited. Parents completed an Infant-Toddler Social and Emotional Assessment (ITSEA; Briggs-Gowan & Carter, 2000) and Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P; Gioia, Espy, & Isquith, 2003). All children were administered a Mullen Scales of Early Learning (Mullen, 1995), and children with ASD were administered the Autism Diagnostic Observation Schedule, Second Edition (Lord et al., 2013) and the Childhood Autism Rating Scale, Second Edition (CARS2; Schopler, Van Bourgondien, Wellman, & Love, 2010). Two 15-minute play samples were conducted with a parent and unfamiliar adult. Play samples were blind-coded using the ERAA and SAP-O (SCERTS model; Prizant, Wetherby, Rubin, & Laurent, 2003). ER symptoms were analyzed across play context (joint interactive play, independent play, disruptive play) and play partner (parents and strangers).

Results: The ERAA produced near-perfect reliability, with Cohen's kappa values resting at .81. The ERAA significantly distinguished children with typical development from children with ASD, $t(60) = 7.20$, $p<.001$. A significant correlation between the ERAA and ASD symptoms was also found, $r(31) = .51$, $p<.01$, indicating that more children with more autism symptoms demonstrated more difficulty regulating emotion. A significant three-way interaction was found among play context, partner, and diagnosis, with independent play with a stranger resulting in more ER difficulties. However, joint-interactive and disruptive play resulted in more discrepant scores between diagnostic groups, despite the overall lower ERAA score. A significant relationship was not found between the ERAA and the ITSEA, suggesting the measurement of different constructs. Executive function skills did not contribute significantly to ER difficulties.

Conclusions: Implications for the current study suggest that emotion regulation symptoms are separate and unique from ASD symptoms. Data suggest that independent play should be further explored in ASD, while disruptive interactions may not be as troublesome as previously reported. Given the results of the current study, the ERAA is a promising tool for assessing emotion regulation in young children and may aid in intervention planning.

**120.096 96** Effects of Depressive Symptoms in Mothers of Children with ASD on Synchrony with Later-Born Infants. B. C. Gamber* and A. R. Neal-Beevers, *University of Texas at Austin*

Background: It has been established that maternal functioning is related to optimal caregiving for children in general, and that mothers of children with ASD often experience elevated symptoms of depression, anxiety, and stress (e.g., Duarte et al., 2005). However, it is unclear how these symptoms might affect their interactions with later-born children (SIBS-ASD) who are at increased risk for ASD. Siller and Sigman (2002) created a quantitative behavioral measure of mother-child synchrony, the proportion of a mother's interactions that are sensitive toward and contingent upon her child's focus of attention.

In this study, we hypothesized that mothers of SIBS-ASD would report higher depressive symptoms than mothers of infants with a typically-developing sibling (SIBS-TD). We also hypothesized that depression scores would be negatively associated with synchrony across groups, but that this effect would be strongest for mothers of SIBS-ASD.

Objectives: This study is the first to examine possible associations between maternal depressive symptoms and synchrony during mother-infant interactions for mothers of children with ASD versus mothers of children without ASD.

Methods: Nineteen SIBS-TD (9 female), 11 SIBS-ASD (6 female), and their mothers were recruited as part of a larger longitudinal study. Data were collected when infants were approximately 12 months old. Each mother-infant dyad engaged in a 15-minute unstructured play session with a standardized set of toys. Free play was coded for synchrony yielding the proportion of: maternal indicating behaviors synchronized with infant attention (MS1), maternal utterances synchronized with infant attention (MS2), and maternal utterances synchronized with infant attention & action (MS3). Mothers also completed a self-report measure of depression symptoms (Center for Epidemiological Studies Depression Scale; Radloff, 1977).

Results: A one-way ANOVA revealed significantly higher depression scores for mothers of SIBS-ASD (M=14.82) versus mothers of SIBS-TD (M=6.13), $F(1,25) = 8.97$, $p < .01$. There were no significant differences between groups for MS1, MS2, or MS3. Multiple linear regressions indicated a significant interaction effect between sibling risk group and maternal depression on MS2 and MS3. A similar trend was observed for MS1, though the interaction was not statistically significant.

Conclusions: These preliminary results replicate previous findings of increased depression symptoms for mothers of children with ASD. Furthermore, while there was no main effect for sibling diagnosis or maternal depression on synchrony scores, there was an interaction effect. Higher maternal depression scores predicted lower mother-infant synchrony, but only for mothers of SIBS-ASD. Thus, depressive symptomatology in mothers of children with ASD is an important factor affecting interactions with their later-born infants. With additional data at 12, 15, and 18 months, we will examine the relationship between synchrony and measures of maternal functioning over time, and how this differs for families affected by ASD. Enhanced understanding of these transactional processes has the potential to inform research and clinical practice for families affected by ASD, such as enhancing the outcomes of parent training interventions.

**120.097 97** Screening Versus Surveillance: Differences in Demographic, Developmental, and ASD Symptom Profiles. K. A. Casagrande*, K. A. Haynes and D. Robins, *Georgia State University*

**Background:** The increasing prevalence of Autism Spectrum Disorder (ASD) has resulted in greater awareness and stressed the importance of ASD specific screening and surveillance. African-American children are less likely to be referred by pediatricians, and are diagnosed as much as 2 years later than Caucasian peers. Additionally, it has been shown that many primary care physicians do not engage in routine ASD screening. As early intervention improves the prognosis for children with ASD, it is important to address the gap in referral and diagnosis for children from minority backgrounds. It is also important to examine how surveillance and screening may differ in utility.

**Objectives:** We investigated the demographic, developmental, and ASD symptom profiles of children who are referred for ASD evaluation based on screening positive on the Modified Checklist for Autism in Toddlers (Revised; M-CHAT-R) compared to those who screened negative, but whose pediatrician had ASD concerns based on surveillance. Minority children, or children from lower SES, may be less likely to be referred for ASD by their pediatrician. Additionally, children caught through surveillance may show more severe symptom presentation than those detected through screening, and those detected by both would have the most severe symptoms.

**Methods:** In our study, participating pediatricians distributed the M-CHAT(-R) during 18- and 24-month well-child visits (screening) and indicated whether they have concerns about the child's development (surveillance). Developmental and ASD symptom profiles were examined for 208 children at risk for ASD: 155 from screening alone (SCR), 24 from surveillance alone (SURV), and 29

from both screening and surveillance (S+S). Evaluations consisted of measures of ASD symptomatology, general cognitive skills, and adaptive abilities.

**Results:** On measures of ASD symptomatology, children identified by S+S were more severe (CARS total score: *M*=32.05 *SD*=5.73; ADOS severity score: *M*=5.79, *SD*=2.48) than those identified by SCR (CARS total score: *M*=26.78 *SD*=6.86, *p*=.001; ADOS severity score: *M*=3.95 *SD*=2.53, *p*=.001); differences between S+S and SURV were not significant (*p*s>.056).

On cognitive, language, and adaptive measures, children detected by S+S (VABS Communication: *M*=75.59 *SD*=4.14; VABS Socialization: *M*=81.52 *SD*=10.02; MSEL Receptive Language: *M*= 25.62 *SD*=10.06) were more impaired than those detected by SURV (VABS Communication: *M*=86.63 *SD*=11.36, *p*=.011; VABS Socialization: *M*=89.54 *SD*=12.43, *p*=.018; MSEL Receptive Language: *M*=35.04 *SD*=14.51, *p*= .021). Additionally, on measures of socialization, children detected by SCR (VABS Socialization: *M*=83.28 *SD*=10.21) were more impaired than those detected by SURV (*p*=.021).

Children identified through S+S or SURV (n=53) had higher levels of maternal education (*t*(198)=3.32, *p*=.001) and were more likely to be Caucasian ($\chi^2$(1,208)=4.61, *p*=.032) than those who were identified by SCR (n=155); however, Caucasian children were not more likely to be diagnosed with ASD than their African-American peers ($\chi^2$(1,208)=.56, *p*=.46) and level of education did not differ significantly based on diagnosis (*t*(198)=1.79, *p*=.075).

**Conclusions:** These results suggest that increased diagnosis among Caucasian and high SES families and later diagnosis of African-American children may be an artifact of differences in referral rates, not an actual difference in prevalence. Integrating screening and surveillance for the identification of ASD maximizes detection of children.

**120.098 98** Diagnostic Stability from Age 3-8 Years in a Canadian High-Risk Sibling Cohort. J. A. Brian*[1], S. E. Bryson[2], I. M. Smith[3], C. Roncadin[4], W. Roberts[5], N. Garon[6], P. Szatmari[5] and L. Zwaigenbaum[7], (1)*Holland Bloorview Kids Rehab/ University of Toronto*, (2)*Dalhousie/IWK Health Centre*, (3)*Dalhousie University / IWK Health Centre*, (4)*Peel Children's Centre*, (5)*University of Toronto*, (6)*Mount Allison University*, (7)*University of Alberta*

Background: Prospective study of high-risk infants in longitudinal designs affords the opportunity to characterize the earliest signs of ASD and investigate their developmental course. Given relatively high rates of ASD diagnosis at age 3 in our cohort (26.6%; Zwaigenbaum et al., 2012), the stability of diagnosis has become an important issue.

Objectives: To examine diagnostic stability, from 3 to 8 years of age, using longitudinal data from a high-risk cohort of younger siblings of children with ASD.

Methods: Participants were 51 high-risk infants (HR; younger siblings of children with ASD) followed from age 6-12 months to at least 8 years, drawn from our larger study. Blinded, clinical best estimate (CBE) diagnoses were made at 3 and 8 years, informed by the ADI-R, ADOS and DSM-IV-TR. Chi-Squared and Cohen's Kappa were used to assess diagnostic stability across the two time points; file review provided additional details about children whose diagnoses were not stable across time points.

Results: Overall agreement between 3- and 8-year CBE diagnosis was good (Kappa = .64, p<.001). Of 51 high-risk infants followed to age 8, 14 received an ASD diagnosis at age 3 (27.4%; 12 male). By age 8, 12/14 retained their ASD diagnosis (85.7%; 11 male), and an additional 6 received a new diagnosis of ASD (3 male, 3 female); 31/37 retained their non-ASD status (83.8%). Of the two cases who ostensibly "lost" their 3-year ASD diagnosis, one (male) was judged to be "non-ASD" at age 5, but retained "other" (sub-threshold) ASD-related concerns at 8; the other (female) was characterized as having Asperger syndrome at age 5, but by age 8 was described as non-ASD with language and learning challenges. Of the six "new" ASD cases, 3 received an ASD diagnosis at age 5 (2 females had language delays and 1 male had "other/behavioural" concerns at 3). The remaining 3 cases (2 males, 1 female) had demonstrated "other" concerns at age 3 or 5 (e.g., social anxiety, behavioral inflexibility). The "new" diagnoses at 8 covered the full DSM IV spectrum (2=Autism; 2=Asperger syndrome; 2=ASD/PDD-NOS).

Conclusions: To our knowledge, this is the first report of stability and change in diagnosis from 3 to 8 years in a prospective high-risk infant sibling cohort. Only 2 children diagnosed with ASD at age 3 did not retain that diagnosis at age 8, although developmental concerns continued to be evident for both. Of the 6 cases not identified as ASD at age 3, three received that diagnosis at age 5 and the remainder at age 8. In all of these cases, other social, language and/or behavioural concerns had been identified by 3 or 5. Discussion will explore further the cognitive, learning, and language profiles, as well as ASD symptomatology of cases whose diagnoses changed. These findings highlight the relative stability of early diagnosis, but also shed light on factors that may contribute to variability in the emergence and expression of ASD between age 3 and 8.

**120.099 99** Communication Spontaneity in Response to Direct Social Prompts Predicts ASD Symptoms in High and Low Risk Infants. S. L. Alvarez*[1], A. Estes[1], B. LeBlanc[2], T. St. John[3], S. Dager[1] and .. The IBIS Network[4], (1)*University of Washington*, (2)*University of Oregon*, (3)*University of Washington Autism Center*, (4)*Autism Center of Excellence*

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**Title:** Communication Spontaneity in Response to Direct Social Prompts Predicts ASD symptoms in High and Low Risk Infants

**Background**: Children with ASD demonstrate a unique profile of early communication behaviors. One aspect of early communication development that has received limited attention is Communication spontaneity (CS). CS has been conceptualized as the level of environmental support required for a child to initiate a communication act. CS has been identified as an important component of functional communication. However, there is limited consensus on how to best define and measure CS. Additional research is needed to understand the nature of CS (i.e., descriptive data across populations and ages) and its relevance to developmental outcomes.

**Objectives:** This study examined CS in a cohort of infants with an older sibling with ASD (high-risk; HR) and infants with typically developing older siblings (low-risk; LR). The purpose is to:

(1) provide the first descriptive data on CS in a longitudinal sample of children at 12 and 24 months, (2) describe the relationships between CS and language and developmental outcomes among 4 groups of children: HRNonASD, HRASD, LRNonASD, LRASD,

(3) determine if (a) 12-month CS predicts ASD symptoms at 24 months and (b) the relationship between CS and ASD symptoms differed by prompting condition, and

(4) examine whether CS changes between 12 and 24 months differ by group.

**Methods:** Participants are part of a larger, multi-site, prospective infant sibling study (NIH IBIS ACE Network) examining brain and behavioral development. We examined a subsample of HR (n=50) and LR (n=31) infants from the University of Washington. To measure CS, videos of the CSBS:DP were blindly coded using a newly-developed coding system capturing the level and type of prompting required for a child to initiate communication acts.

**Results:** CS was associated with language and social communication abilities. Social context, specifically, child response to direct, social prompts during the CSBS-DP at 12 months of age, was associated with ADOS diagnostic group and symptom severity at 24 months controlling for initial language abilities. Unaffected, HR siblings also demonstrated lower CS during the direct social prompt condition than LR siblings, at 24 months.

**Conclusions:** This study was the first to prospectively measure CS in infants at 12 and 24 months. Lower CS at 12 months was associated with increased symptoms of ASD and a greater likelihood of meeting ADOS criteria for ASD at 24 months. The context of social communication was found to be an important consideration. No group differences in CS were evident during free play or indirect environmental prompts. However, group differences in level of CS were found in response to direct social prompts. Thus, social prompt responsiveness (SPR) at 12 months uniquely predicted later ASD symptoms. Assessing SPR in HR infants may shed light on a new dimension of social communication deficits in ASD and lead to new intervention targets for very young children prior to the diagnosis of ASD.

**120.100 100** The Effect of Target Saliency on the Disengage Deficit in a Reaching Task in Autism Spectrum Disorder. L. A. R. Sacrey*[1], T. Germani[1], S. E. Bryson[2] and L. Zwaigenbaum[1], (1)*University of Alberta*, (2)*Dalhousie/IWK Health Centre*

**Background**: It is widely reported that persons with Autism spectrum disorder (ASD) have disordered visual attention, in that they tend to continue looking at a target long after typically developing peers look away (i.e., a 'disengage deficit'). During toy play, toddlers at high-risk (HR) of ASD (i.e., with an older sibling diagnosed with ASD) show a disengage deficit when grasping toys (Sacrey et al., 2013). Interestingly, resent research has noted that target saliency may impact visual attention patterns of persons with ASD (Freeth et al., 2011), raising the question of whether saliency may influence disengagement of attention in HR infants.

**Objectives**: To determine if target saliency affects latency to disengage visual attention in HR infants during a reaching and grasping task.

**Methods**: *Participants*: Three groups of toddlers: (1) HR siblings who did not receive an ASD diagnosis at 36 months (HR-N), (2) HR siblings who did receive a diagnosis of ASD at 36 months (HR-ASD), and (3) toddlers without a family history of ASD (low-risk; LR).

*Task*: LR and HR were filmed at 18, 24, and 36 months of age as they engaged in play with small, easily graspable toys (high visual saliency) or ate small, easily graspable food items (low visual saliency). Duration of time spent looking at targets before moving the hand towards the target (engaging attention) and the duration of time spent looking at the target after grasp (disengaging attention) were measured and transformed into percentage of time.

*Diagnostic Assessment:* At 36 months of age, an independent diagnostic assessment for ASD (including ADOS, ADI-R and clinical judgment based on DSM-IV-TR) was completed for all participants.

*Statistical Analyses*: A 3 (**Group**: LR, HR-N, HR-ASD) x 3 (**Age**: 18, 24, 36 months of age) x 2 (**Target**: toy, food) repeated measures ANOVA was completed on measures of engaging attention and disengaging attention.

**Results**: For engaging attention, the HR groups spent more time staring at the target than LR before reaching towards it (HR-ASD=19.8%; HR-N=12.8%; LR=4.3%; *ps*<0.0167). There were no target effects; that is, percentage of time looking at the target prior to reaching did not differ between the toy and food targets (14.5% versus 10.7%, respectively). For disengaging attention, the HR-ASD spent more time staring at the target than the LR group (HR-ASD=23.3%; HR-N=13.7%; LR=2.9%; p=0.001) following grasp. In addition, the LR (22.3%; *p*=0.002) and HR-N (19.5%; *p*=0.006) groups were more likely to disengage from the target at tactile contact than was the HR-ASD (8.4%) group. There was a target effect, in that all groups were more likely to continue looking at a toy target following grasp than a food target (17.2% versus 9.5%, respectively; p=0.002).

**Conclusions**: The results suggest that target saliency does not have an ASD-specific effect on engaging and disengaging visual attention during reaching for food and toys in LR and HR toddlers. As such, the disengage deficit present in HR-ASD toddlers may serve as an early behavioural marker for ASD.

**120.103 103** Do Clinicians Operationalize the Broader Autism Phenotype the Same Way Across Sites?. A. Vehorn*[1], K. Gotham[2], L. V. Ibanez[3], W. L. Stone[3], D. S. Messinger[4] and Z. Warren[2], (1)*TRIAD, Vanderbilt Kennedy Center*, (2)*Vanderbilt University*, (3)*University of Washington*, (4)*University of Miami*

Background: Many researchers and clinicians have started to utilize the term and concept of a 'Broader Autism Phenotype (BAP)' in an attempt to better understand the complex etiology, genetic/familial contributions, developmental trajectories, and range of outcomes associated with siblings of children with Autism Spectrum Disorders (ASD). To use the term effectively, however, we must establish shared operational definitions and methods for assessing the BAP at various points in development. At this point, it is unclear whether clinicians across sites identify BAP concerns based on the same symptoms and profiles.

Objectives: To examine variables associated with clinician-rated BAP in siblings of children with ASD and typically-developing controls and investigate the relative emphasis placed on these variables across three clinical research sites.

Methods: N=88 toddlers (N=45 sib-ASD, N=43 control) aged 36 months (Mullen ELC M=108.7, SD=16.9) were assessed at three clinical research sites collaborating on a prospective study of infant sibling development. No children receiving a diagnosis of ASD (N=12) were included in analyses. As part of a best-estimate diagnostic procedure, clinicians blind to group status rated whether they had BAP concerns (yes/no). This was done for both siblings of children with ASD and controls. If "yes" to BAP concern, clinicians specified their concern (yes/no) on the following domains: Social, Language/Communication, Atypical Behaviors, Emotional/Behavioral , or Discrepancy between observed and reported behavior. Data also were available from the Autism Diagnostic Interview-Revised (ADI-R; Rutter, Couteur & Lord 2005), the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000), Vineland Adaptive Behavior Scales, 2nd edition (Vineland II; Sparrow et al., 2005), and the Mullen Scales of Early Learning (MSEL; Mullen, 1994). Logistic regression models were used to examine which continuous scale scores and binary clinician-rated symptom domain variables were associated with BAP concerns, with and without controlling for site.

Results: Across all sites, the presence of BAP concern was significantly associated with the ADOS Social Affect and Restricted Repetitive Behavior domain scores, the Mullen Early Learning Composite, and the Vineland-II Socialization and Communication domain scores. Out of 34 children with identified BAP, clinicians were concerned about language and communication functioning for 56%, and about social and atypical behaviors for 41% respectively, with 12% eliciting concern over other emotional/behavior symptoms. In 6% of these children, a discrepancy was noted between observed and reported behavior. No predictor-by-site interactions were significant for either these binary BAP domain ratings or the continuous variables. Some 20% (N=8) of these children rated as having BAP concerns were from the non-sib control group.

Conclusions: Binary ratings of BAP may represent ratings of meaningful subclinical concerns, as they are correlated with commonly used phenotyping measures across sites. Our findings suggest that these ratings were not different across three clinical sites although clinicians were given no specific training in overall BAP appraisal. However, the content and meaning of these subclinical concerns warrants substantial consideration. A majority of concerns related to language, and children with no family history were often rated as evidencing BAP concerns.

**120.104 104** Project Impact: Examining Mothers' Scaffolding Techniques during Play in Toddlers with ASD. J. M. Pierucci*[1], A. B. Barber[2] and A. T. Gilpin[3], (1)*St. Mary's University*, (2)*University of Alabama ASD Clinic*, (3)*University of Alabama*

**Background:** Vygotsky (1962) coined the phrase "scaffolding", which occurs when an individual is provided enough support to learn (i.e., progressing from actual level to potential level of development). Play is an important learning platform for children, in which they have opportunities to both learn and practice skills (e.g., language, social, etc.). Considering scaffolding in the context of play, parents' involvement in children's actual developmental level could foster growth toward children's potential developmental level. Children with (ASD), given frequently reported delays in play skills, could benefit from parents scaffolding their play.

Researchers have demonstrated that parents of children with typical development scaffold the development of play beginning at 12 months through the preschool years using the following techniques: (1) comments, (2) requests, and (3) prompts (Woolley & Tullos, 2008). Currently, no research has examined these scaffolding techniques in toddlers with ASD.

**Objectives:** The aims of the current study were to examine: (1) mothers' scaffolding techniques (i.e., comments, requests, and prompts) during mother-toddler play samples, and 2) toddlers' social engagements (i.e., attention, nonverbal, and verbal responses) to mothers' scaffolding techniques.

**Methods:** The current study was a single-subject A-B intervention design that implemented a social-communication intervention (i.e., Project ImPACT: Improving Parents As Communication Teachers) for toddlers with ASD ($n$ = 3; 2 males and 1 female; $M$ = 26.5 months, $SD$ = 3.8; range = 22.3 – 29.8 months at start of intervention). Toddlers and their parents participated in 5 baseline sessions and 12 intervention sessions and attended 2 group sessions each week during

9 consecutive weeks. During the parent-group intervention sessions, mothers learned Project ImPACT teaching techniques. Trained coders measured: 1) the use of mothers' scaffolding techniques, and 2) toddlers' social engagements in scaffolding techniques from video recordings of each mother-toddler play sample.

**Results:** Simulation Modeling Analysis (SMA) was used to compare frequencies of behaviors (i.e., mothers' scaffolding techniques and toddlers' social engagements) from baseline to intervention sessions. The following highlights the significant changes for each participant in level vector change from baseline compared to level vector change from intervention:

$P_1$ comments: $r$ = .902**; $P_1$ requests: $r$ = -.925**; $P_1$ prompts: $r$ = .775*

$P_2$ comments: $r$ = .878**; $P_2$ requests: $r$ = .873**; $P_2$ prompts: $r$ = .856**

$P_3$ comments: $r$ = .384; $P_3$ requests: $r$ = -.788*; $P_3$ prompts: $r$ = .719*

Although findings were individually interpreted for each participant, overall results from Simulation Modeling Analysis (SMA) showed that mothers' scaffolding techniques changed significantly from baseline to intervention. Additionally, toddlers' social engagements to these techniques significantly improved from baseline to intervention. Toddlers' social engagements for each scaffolding techniques will be presented. *Note*. *$p$ < .05, **$p$ < .005.

**Conclusions:** These findings suggest that Project ImPACT was an effective intervention in training parents with useful scaffolding techniques. Secondly, findings highlight the importance of scaffolding children's actual development to lead to their potential development. Overall, these data emphasize the essential role parents fulfill as early interventionists for their toddlers.

**120.105 105** Regression in Children with ASD: Associations with Parents' Beliefs about Causes of ASD. R. P. Goin-Kochel*[1], S. S. Mire[2] and A. G. Dempsey[3], (1)*Baylor College of Medicine*, (2)*University of Houston*, (3)*University of Texas Health Sciences Center*

Background: Parent-reported developmental regression occurs in an average of one-third of children with autism spectrum disorder (ASD). While prospective, clinician-rated studies detect higher rates of skill losses, understanding *parent perception* of this phenomenon is valuable, as it may subsequently color parents' thoughts about ASD and decisions they make on behalf of their families. Limited data suggest that parents who observed regression in their children were significantly more likely to believe that external factors—most often vaccines—caused ASD (Goin-Kochel & Myers, 2005). Fears about immunizations causing autism is now one of the leading reasons behind a growing trend of delayed or refused vaccine uptake (Offit, 2008), which has important public-health ramifications (e.g., increased disease outbreaks). Understanding more about how regression shapes parents' beliefs and actions is key to developing targeted education efforts.

Objectives: (a) To provide descriptive information about regression status across three related samples; (b) To assess parents' degree-of-agreement with various potential causes of ASD; and (c) To determine whether child history of regression is associated with beliefs about causes of ASD.

Methods: Data were analyzed for children with ASD (probands; $N$=2758; $M$ age=9 years, $SD$=3.6 years, range=4—17.9 years) who participated in the Simons Simplex Collection (SSC). Regression was defined according to the *Autism Diagnostic Interview—Revised* (ADI-R), with rates of language and social-skill losses calculated for the full SSC sample; SSC probands from the Baylor College of Medicine (BCM) site ($n$=203); and a subset of BCM probands who were recontacted for additional data collection ($n$=68), including parents' beliefs about causes of ASD via the *Revised Illness Perception Questionnaire* (IPQ-R; Moss-Morris, et al., 2002). Frequencies of agreement/disagreement with possible ASD etiologies were calculated for the IPQ-R's 21 closed-ended items about potential causes. Qualitative analyses were used to categorize parents' open-ended rankings of their top three beliefs about causes of ASD. ANOVA's were conducted to determine whether parents' degree-of-agreement with various etiologies differed according to their child's regression status.

Results: Regression rates were only slightly higher in the BCM samples: full SSC=29.5%, full BCM=34%, recontacted BCM=35.3%. The five causes that families most frequently endorsed

were genetics (75.8%), child's brain structure (59.7%), will of God (46.3%), toxins found in vaccines (41.8%), and environmental pollution (37.4%). Parent-provided causes were organized into 10 categories, with genetics/heredity being first-ranked among the largest proportion of parents (42.6%); however, external factors were ranked (i.e., 1st, 2nd, or 3rd) by nearly 84% of families as causing ASD. Parents who reported regression in their children were more likely to agree with "toxins in vaccines" ($F$[1,66]=3.74, $p$=.05) and "environmental pollution" ($F$[1,66]=3.25, $p$=.07) as causes.

Conclusions: Findings support an association between parent-reported regression in children with ASD and parental endorsement of vaccines/external mechanisms as causing autism, even within this small subsample. That so many also endorsed "will of God" may reflect potential geographical and/or cultural differences within the BCM subsample. Replication of this study at other SSC sites will elucidate varying belief patterns by locale for targeted education efforts.

**120.106 106** Imitation and Joint Attention As Predictors of Language Outcome in Infants at High and Low Risk for ASD. S. R. Edmunds*, L. V. Ibanez and W. L. Stone, *University of Washington*

Background: Language development requires the coordination of many early abilities. Motor imitation and responding to joint attention (RJA) are two early emerging behaviors that have been found to predict later expressive language ability in both typically developing (TD) children and those with ASD (Charman et al., 2000; 2003; Morales et al., 2000; Stone et al., 2001). Theory suggests that imitation promotes increased RJA behaviors because imitative play encourages infants to follow the attention of others for further imitation opportunities (Ingersoll et al., 2008; McDuffie et al., 2007). In turn, RJA skills are thought to facilitate language learning by increasing the infant's ability to map language onto another person's referent (Akhtar et al., 1996; Baldwin, 1995). In this study we propose and test a mediational model of language development in which the longitudinal relation between imitation and expressive language is mediated by infants' ability to respond to joint attention bids. To examine this pathway while these behaviors are first emerging, we study infants at elevated risk for ASD (i.e., infant siblings of children with ASD; HR infants) and their low-risk peers (LR infants). We predict that the directionality of the mediational pathway will be similar for the two groups. In light of previous studies finding stronger concurrent associations between these abilities for ASD than TD children (Mundy et al., 1990), we also predict that the mediation effect will be stronger for HR infants.

Objectives: To examine a mediational model of the longitudinal relations between imitation, RJA, and expressive language in both HR infants and LR infants.

Methods: The sample comprised 63 infants (HR $n$=38; LR $n$=25) who were assessed at 12, 15, 24, and 36 months of age through a longitudinal multisite study. Motor imitation was measured at 12 months using the Screening Tool for Autism in Toddlers (STAT; Stone et al., 2008), RJA was measured at 15 months using the Early Social Communication Scales (ESCS; Mundy et al., 2003), and expressive language was measured at 24 months using the Mullen Scales of Early Learning (MSEL; Mullen, 1995).

Results: To conduct the mediation analysis, simple and conditional indirect effects were assessed using the PROCESS macro with bias-corrected, bootstrap-generated confidence intervals (10,000 samples; Hayes, 2013). As hypothesized, RJA mediated the relation between imitation and language such that: (1) 12-month imitation predicted 15-month RJA ($R^2$=.09, $F$(1,61)=5.90, $b$=1.07, $p$<.02); (2) 15-month RJA predicted 24-month expressive language controlling for 12-month imitation ($R^2$=.18, $F$(2,60)=6.49, $p$<.01); and (3) the indirect effect was significant, as the confidence interval did not include zero ($c'$=2.25, *95% CI* [.35, 5.44]). Contrary to prediction, the strength of the mediation pathway was comparable for HR and LR infants.

Conclusions: These findings support the idea of a developmental sequence in which infants' early imitation ability leads to higher levels of later expressive language in part through their intermediate RJA behaviors. The strength of the mediation is similar for both risk groups, which suggests that infants share a common developmental pathway. Further analyses will be conducted as coding of all behaviors and diagnostic visits continue.

**120.107 107** The Relationship Between Autism Symptoms and Arousal Level in Toddlers with ASD, As Measured By Electrodermal Activity. E. B. Prince*[1], E. Gisin[2], C. A. Wall[1], K. Chawarska[1] and F. Shic[1], (1)*Yale University School of Medicine*, (2)*Penn State Hershey College of Medicine*

Background:
Electrodermal activity (EDA) is a measure of skin conductance and is often used to determine the level of emotional arousal in children and adults (Dawson, 2000). Previous studies have examined EDA in the context of face recognition, gaze direction and eye contact in children and adults with Autism Spectrum Disorders (ASD) using EEG and eye-tracking protocols (Joseph, Ehrman, McNally, & Keehn, 2008; Kylliainen & Hietanen, 2006; Kylliainen et al., 2011). However, little is known about EDA in toddlers with ASD and even less is known about it during real-world behavioral assessments.

Objectives:
To use EDA measurements to examine differences in reactivity between toddlers with ASD and their typically developing (TD) peers during a behavioral assessment of social communication.

Methods:
21 toddlers (10 TD, 11 ASD; mean age=22 months) received the Communication and Symbolic Behavior Scale (CSBS) as part of a comprehensive assessment of social functioning, communication skills, and development. The CSBS comprises a number of activities designed to elicit social and communicative behaviors in toddlers. These include interaction with animal figurines, toy cars, books, wind-up toys, bubbles, balloons, and a snack session. The activities were grouped into four categories: books, animals, mechanical toys, and temptation episodes. During the 30 minute session, participants wore a sensor on their ankle (Affectiva Q-Sensor) that measured EDA in microsiemens at 8 Hz. The first second of each activity was used as a baseline measure. We used the largest absolute change to identify the magnitude of change from baseline during each activity.

Results:
We used a 2 (diagnosis) by 4 (activity) mixed factorial design and ran a linear mixed models ANOVA. Because the children were likely to vary in verbal abilities based on diagnostic group, we controlled for Verbal DQ scores as measured on the Mullen Scales of Early Learning. In TD toddlers, there was a significant difference in the absolute change in EDA between the animal toys and the temptation tasks ($p<0.05$). However, this was not the case in children with ASD. For these children, there was a significant difference in EDA between the animal toys and the mechanical category which includes cars, helicopters, spinning and wind-up toys ($p<0.01$).

Conclusions:
Children with ASD have a dissimilar reaction to activities on the CSBS as compared to their typically developing peers. Both groups responded similarly to the animal toys, which are generally the least exciting and interactive items. However, while TD children showed a greater change in EDA during the "temptation" toys which require them to interact with the examiner in order to operate the object, those with ASD showed a heightened response to mechanical toys. These results are consistent with previous findings demonstrating that children with ASD are more likely than TD children to have a circumscribed interest in mechanical systems (Turner-Brown, Lam, Holtzclaw, Dichter, & Bodfish, 2011). These preliminary results offer physiological evidence of arousal differences between toddlers with ASD and their typical peers upon presentation of specific stimuli.

**120.108 108** Sub-Threshold Autism Symptomatology at Age 2 Is Predictive of Movement Onto the Autism Spectrum at Age 4. E. Moulton*[1], D. A. Fein[1], M. L. Barton[1], D. Abrams[2] and D. Robins[2], (1)*University of Connecticut*, (2)*Georgia State University*

Background:

Symptoms of Autism Spectrum Disorders (ASD) are widely thought to emerge by 12 months in some children. This allows for reliable diagnosis as early as 16 months in these children. Another group of children, however, may not meet symptom criteria until later in the toddler or preschool years. Little is known about this group of children who may receive a non-ASD diagnosis before receiving an ASD diagnosis. Are these children simply misdiagnosed or missed early in toddlerhood? Or do they represent a subset of the ASD population who do not show the full disorder until three or four years of age?

Objectives:

To enhance our understanding of the subset of children who appear to move onto the autism spectrum between ages two and four.

Methods:

Following positive screening on an autism-specific screening questionnaire (M-CHAT(-R)) between 16 and 30 months, 102 children were evaluated and determined to not meet criteria for an ASD. Of these children, 38% received a diagnosis of Developmental Delay, 22.5% received a diagnosis of Developmental Language Disorder, 23.5% received no diagnosis (no DSM diagnosis was met, but development was not typical), 8.8% were typically developing, and 6.9% received other diagnoses (e.g., Motor Delay). The Autism Diagnostic Observation Schedule (ADOS), Mullen Scales of Early Learning, Vineland Adaptive Behavior Scales, and Childhood Autism Rating Scale (CARS) were completed. Diagnostic determination was made based on the clinical judgment of experienced clinicians.

Results:

At follow-up at approximately 48 months, 90 children (88%) remained off the spectrum (NonASD-NonASD) and 12 (12%) received an ASD diagnosis (NonASD–ASD). A Chi-square test for independence indicated no significant association between initial diagnosis and movement onto the spectrum ($p$=.671). The children who moved onto the spectrum were matched to peers who retained a non-ASD diagnosis in terms of gender, age and diagnosis at age two. Independent groups $t$-tests were used to compare age two CARS and ADOS ratings of the NonASD-ASD group (N=12) to the NonASD-NonASD group (N=24). No significant group differences were found in ADOS domain scores. The NonASD-ASD group was found to have significantly ($p$=.031) higher CARS total scores ($M$=24.50,$SD$=4.34) than the NonASD-NonASD group ($M$=21.48,$SD$=3.21). Specifically, the NonASD-ASD group showed poorer nonverbal communication ($p$=.032) and more abnormal visual response ($p$=.007). Importantly, however, symptomatology was well below diagnostic threshold for both groups. Individual ADOS items were investigated in these areas, and the NonASD-ASD group was found to have ($p$=.044) poorer response to joint attention ($M$=.90,$SD$=.57) than the NonASD-NonASD group ($M$=.30,$SD$=.99).

Conclusions:

Movement from a non-ASD diagnosis to an ASD diagnosis between 24 and 48 months occurs for a small subset of children (12% of children who screened positive on M-CHAT but were not diagnosed with ASD). Initial diagnosis does not appear to predict movement onto the spectrum. Children who move onto the spectrum exhibited greater autism symptomatology at age two than children who remained off the spectrum. This indicates that sub-threshold autism symptoms may help to predict this relatively rare occurrence. Further analyses will investigate additional factors that may help to characterize this group.

**120.109 109** The Relationship Between Rhythmic Movement and Babble Onset in Infants at Heightened Risk for ASD. K. L. West*, N. B. Leezenbaum, J. B. Northrup and J. M. Iverson, *University of Pittsburgh*

Background: In typically-developing infants, the onset of reduplicated babble (i.e., vocalizations with repeated consonant-vowel sequences; [bababa]) is accompanied by a significant increase in rhythmic motor activity in the upper limbs (e.g., shaking, banging; Iverson et al, 2007), suggesting coupling of the vocal and motor systems. However, research examining these behaviors in the infant siblings of children with autism spectrum disorder (ASD; High Risk; HR) finds that this relationship is attenuated relative to infants without an older sibling with ASD (Low Risk; LR; Iverson & Wozniak, 2007). It is possible that instability of the vocal and motor systems in the subset of HR infants who go on to have ASD accounts for differences between LR and HR infants; however, this hypothesis has yet to be tested.

Objectives: The present study was designed to examine change in rhythmic movement at babble onset in LR infants and in three groups of HR infants: No Diagnosis, Language Delay, and ASD.

Methods: Participants included 52 HR infants who were videotaped at home monthly from 5-14 months. A comparison group of 30 LR infants was observed bi-weekly from 2-19 months. Sessions for both samples consisted of 45 minutes of naturalistic and semi-structured play. The present study focused on the visits one month prior to and

at the onset of reduplicated babbling. Babble onset was identified using parent report and experimenter observation. All instances of rhythmic movements (i.e., movements repeated in the same form at least 3 times within intervals of 1sec; Thelen, 1979) were coded, and rates of rhythmic movement per 10 minutes were calculated.

At 36 months, HR infants received a diagnostic evaluation using the ADOS-G (Lord et al., 2000) and clinical judgment. Eight HR infants received an ASD diagnosis (HR-ASD). Seventeen HR children with language delays were identified (HR-LD); and the remaining 27 HR infants did not meet ASD or LD criteria (No Diagnosis; HR-ND).

Results: Wilcoxon signed rank tests were used to assess whether rates of rhythmic movement changed significantly from pre-babble to babble onset. Rates of rhythmic movement increased significantly in both the LR ($Mdn_{pre}$ = 3.73, $Mdn_{babble}$ = 6.86) and HR-ND ( $Mdn_{pre}$ = 3.38, $Mdn_{babble}$ = 7.89) groups (*p*'s <.05). A similar increase was also apparent among HR-LD infants ( $Mdn_{pre}$ = 5.08, $Mdn_{babble}$ = 9.23), but the change was only marginally significant (*p*=.068). In contrast, rates of rhythmic movement decreased in the HR-ASD group ( $Mdn_{pre}$ = 12.39, $Mdn_{babble}$ = 10.70), although the change was not significant (Z=-.840, p>.05). Inspection of individual data revealed that 6 of the 8 ASD infants decreased in rate of rhythmic movement from pre-babble to babble onset.

Conclusions: For infants with no diagnosis—regardless of risk status—rhythmic movement significantly increased at babble onset, suggesting a coupling of the vocal and motor systems. Only infants with an eventual ASD diagnosis displayed a different pattern in rhythmic movement, lending support to the hypothesis that disorganization and instability in the vocal and motor systems may be a component of development in ASD.

**120.110 110** Using the M-CHAT-R to Identify Developmental Concerns in a High-Risk 18-Month-Old Sibling Sample. A. S. Weitlauf*[1], A. Vehorn[1], W. L. Stone[2] and Z. Warren[1], (1)*Vanderbilt University*, (2)*University of Washington*

**Background:** With estimates of the recurrence risk of ASD in a younger sibling as high as 18.7% (Ozonoff et al., 2011), identifying early markers of ASD is extremely important for purposes of early diagnosis and intervention. However, screening siblings can also be a complex process that may warrant a more extensive system of identification and testing than current standards dictate. Little is currently known about the sensitivity and specificity of commonly used ASD screening instruments in the general population, much less in the high-risk sibling subset.

**Objectives:** This project examines the predictive properties of a potential community-based measure, the Modified Checklist for Autism in Toddlers-Revised (M-CHAT-R; Robins and Fein, 2011), as a screening instrument for infant siblings of children with ASD.

**Methods:** 71 younger siblings of children with ASD completed M-CHAT-Rs at a mean age of 18 months. Of these children, 25 failed the M-CHAT-R + follow-up interview (FUI). An additional 15 children who passed the M-CHAT-R agreed to participate in full diagnostic evaluations (cognitive, adaptive, and autism testing) for a total of 40 participants. No information is available on participants who failed the M-CHAT-R but declined further evaluation. Three children who failed the screener but passed the FUI did not come in for evaluations.

**Results:** We completed full diagnostic evaluations on 25 children who failed the M-CHAT-R+FUI and 15 children who passed. Diagnoses were as follows: No Diagnosis (ND; n=15), Other Developmental concern (OD; n=3), Autism Spectrum Disorder (ASD; n = 12), and At Risk (AR=10). This At Risk designation included children where the clinician had ASD-related concerns but deferred diagnosis for future evaluation. In ASD and OD, 100% failed the M-CHAT-R+FUI; in AR, 50%; and in ND, 20% of children failed. We examined the M-CHAT-R+FUI sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) two ways. When differentiating between autism risk (ASD+AR), non-autism (OD) and no concerns (ND), the M-CHAT-R+FUI had sensitivity of 77.27%, specificity of 66.67%, PPV of 73.91%, and NPV of 70.59%. When differentiating between *any* developmental concern (ASD, OD, AR) and no concerns (ND), sensitivity and specificity were 80%, PPV was 86.96%, and NPV was 70.59%.

**Conclusions:** The M-CHAT-R+FUI demonstrated better sensitivity, specificity, and PPV when identifying children with any developmental

concern. NPV remained the same across both groups. Differences in sensitivity across groups were modest, whereas differences in the specificity and PPV were larger. Our results mirror Chlebowski et al.'s (2013) finding using the original M-CHAT+FUI in a population-based sample, which indicated that it performed better at picking up general developmental concern (PPV = 98%) than ASD risk (PPV = 54%). Results from our high-risk sample suggest that the M-CHAT-R+FUI continues to pick up broader developmental concerns in addition to ASD-related vulnerabilities, underscoring the need for clinician training to facilitate appropriate post-screening follow-up evaluations for children.

**120.111 111** Parsing Heterogeneity of Early ASD Phenotype: Stability and Change. S. H. Kim*[1], S. Macari[1], C. A. Saulnier[2], A. M. Steiner[3], T. R. Goldsmith[4], J. Koller[5], K. D. Tsatsanis[6] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (3)*Yale University*, (4)*University of New Mexico*, (5)*The Hebrew University of Jerusalem*, (6)*Child Study Center, Yale University School of Medicine*

**Background:** Past studies have consistently found high stability in the diagnosis of Autism Spectrum Disorders (ASD) during toddler years. However, diagnostic stability has not been examined in current cohorts of toddlers for whom intensive interventions are readily accessible. Moreover, due to tremendous heterogeneity observed within ASD early on, knowledge of short-term outcomes is still limited.

**Objectives**: (1) To replicate and extend previous findings on stability of early diagnosis using toddlers from a large clinic-referred sample (born between 2006-2012); (2) To identify more homogeneous subgroups within ASD based on a constellation of key clinical features in the second year of life; (3) To examine short-term outcomes in the identified subgroups at 1-2-year follow-up.

**Methods:** One hundred toddlers referred for a differential diagnosis of ASD at 14-27 months (Time 1) and followed until 30-49 months (Time 2) were evaluated with regard to autism symptoms, verbal and nonverbal skills, and adaptive functioning. At Time 1, we identified homogeneous subgroups within ASD using Hierarchical Clustering (HC) analysis. Developmental outcomes of the identified clusters were compared using generalized linear mixed models. All but one child received early intervention (*Mean*=16.9 hours/week; *SD*=9.16).

**Results:** 94% of children given an ASD diagnosis at Time 1 maintained the ASD diagnosis at Time 2. HC analysis identified 4 clusters at Time 1. Toddlers in clusters 1 and 2 had higher nonverbal and verbal skills and adaptive communication, daily living, and social functioning than toddlers in clusters 3 and 4. Clusters 1 and 2 differed from one another by levels of autism symptoms and nonverbal skills. Clusters 3 and 4 differed in nonverbal, verbal, adaptive social, and daily living skills. Within each cluster, toddlers demonstrated high stability of nonverbal and daily living skills over time. However, changes over time were found within clusters in severity of autism symptoms, verbal, communication, and socialization skills. Specifically, autism severity in cluster 2 increased over time (Cohen's *d*=-1.1) whereas in the three remaining clusters, it remained stable. Verbal and communication skills significantly improved in three clusters (*d's*=1-1.8). However, cluster 4 showed only a modest increase in verbal skills (*d*=0.5) and a decrease (*d*=-0.6) in adaptive communication skills. Finally, cluster 1 showed improvement (*d*=0.6) in adaptive social skills, whereas cluster 4 showed worsening of skills (*d*=-1.4); adaptive socialization for the other two clusters remained stable over time. The clusters differed in the amount of intervention they received between Time 1 and Time 2 with cluster 4 showing the most hours of intervention.

**Conclusions**: High stability of early ASD diagnosis was replicated with the current cohort of toddlers. However, considerable heterogeneity in clinical presentation at 14-27 months resulted in four subgroups whose short-term outcomes also varied. Short-term prognosis was better for children with intact cognitive and adaptive skills early on despite pronounced autism symptoms, especially in terms of progress in verbal and adaptive communication functioning. Identifying subgroups within ASD during toddler years based on multiple clinical features will be crucial for predicting outcomes and programming treatment.

**120.112 112** Play and Playfulness in Young Children with Autism. C. Shulman* and R. Ankori, *Hebrew University in Jerusalem*

Background:

Play, especially "pretend play", is considered of central importance to children's cognitive, social and emotional development (Singer & Singer, 2006). Greenspan and Weider (1998) have argued that the transition to imaginary play represents a major developmental achievement, allowing children to experiment with ideas. Holding both real and imaginative perspectives in mind allows the child self-reflection and the ability to differentiate between subjective and objective experiences. Most children develop the capacity for pretend play when their caregivers are involved in playful interactions. Playfulness has been described as a state of mind in which an individual can think flexibly (Youelle, 2008) and involves intrinsic motivation, internal control, the freedom to suspend reality and framing (Bundy, 1997). Children with autism have been found to be less playful than typically developing children (Hamm, 2006; Muys, Rodger, & Bundy, 2006). In children with autism, deficits in flexibility, imagination and social skills can affect both play and playfulness (Skaines, Rodger, & Bundy, 2006).

Objectives:

This main objective of this study is to examine links between play and playfulness in young children with autism. In addition, correlational analyses between play and playfulness, on the one hand, and cognitive and language functioning, severity of autism symptomotology, and imitation skills, on the other hand, will shed light on the interrelatedness of these two developmental constructs.

Methods:

Forty children with autism spectrum diagnoses based on ADI and ADOS-2, aged 2 ½ to four years old, participated in this study. After diagnostic ascertainment, each participant underwent a comprehensive assessment of cognitive abilities (Mullen Scales), language functioning (PLS), and imitation skills (MIA). Their play and playfulness were assessed in a videotaped 30-minute play session with their mother, which was subsequently coded (Test of Playfulness, Bundy, 1993).

Results:

Playfulness and play were not correlated and each had a specific profile of correlations with the other variables. Both play and playfulness were positively correlated with imitation abilities. Positive correlations emerged between receptive language and playfulness and between expressive language and play. A positive correlation was found between severity of autism symptomology and both play and playfulness, which remained even after controlling for developmental level.

Conclusions:

The present research has introduced playfulness as an additional element to be examined in young children with autism. Although it has several overlapping characteristics with pretend and symbolic play, it also has a unique pattern of correlations with other developmental parameters, such as developmental status, language abilities and imitation. The relationship between playfulness and receptive language as differentiated from the relationship between level of play and expressive language is particularly important in conceptualizing the various interrelated variables affecting the development and interactions of young child with autism with those in their environment. The implications for interventions with young children with autism are discussed.

## 121 Epidemiology

**121.113 113** Exposure to Particulate Matter Air Pollution during Pregnancy Is Associated with Increased Risk of Autism Spectrum Disorder: A Nested Case-Control Study from the Nurses' Health Study II. R. Raz*[1], A. L. Roberts[1], K. Lyall[2], J. E. Hart[1], A. C. Just[1], F. Laden[1] and M. Weisskopf[1], (1)*Harvard School of Public Health*, (2)*UC Davis*

Background: Air pollution contains many toxicants known to affect neurological function and to have effects on the fetus in utero. Airborne particles are covered with biocontaminants, penetrate the subcellular environment and induce oxidative stress and mitochondrial damage in vitro. In rodents, they also stimulate inflammatory cytokine release systemically and in the brain, and alter the neonatal immune system – processes that are implicated in autism spectrum disorder (ASD). Several studies have explored associations of air pollution with ASD, using the US Environmental Protection Agency hazardous air pollutants models, distance to freeway or local models for specific pollutants. These studies suggest increased risk of ASD with higher

exposures to diesel particulate matter (PM), several metals and some organic pollutants as well as closer proximity to a freeway.

Objectives: To explore the association between maternal exposure to PM air pollution and risk of ASD.

Methods: This is a nested case-control study of participants in the Nurses' Health Study II (NHS II), a prospective cohort of 116,430 United States female nurses aged 25-43 when recruited in 1989, followed by biennial mailed questionnaires. Study participants were NHS II participants' children born 1990-2002 with ASD (n=245), and children without ASD (n=1522) randomly selected using frequency matching for birth years. Monthly averages of airborne particulate matter with diameters ≤2.5μm (PM2.5) and between 2.5μm and 10μm (PM10-2.5) were predicted from a spatiotemporal model for the continental US and linked to residential addresses updated every two years.

Results: $PM_{2.5}$ exposure during pregnancy was significantly associated with increased odds of ASD, with the 4$^{th}$ quartile having an adjusted odds ratio of 1.71 (95% CI: 1.10–2.66) in comparison to the 1$^{st}$ quartile. The association was stronger when limiting the sample to those who did not change residences around the time of pregnancy (odds ratio = 2.02, 95% CI: 1.15-3.54). Associations with $PM_{2.5}$ exposure 9 months before or after the pregnancy were substantially lower. There was no association of ASD risk with $PM_{10\text{-}2.5}$.

Conclusions: Higher exposure to $PM_{2.5}$ during pregnancy is associated with risk of ASD. This association is specific to $PM_{2.5}$ and to the pregnancy period.

**121.114 114** Mortality in Persons with Autism Spectrum Disorders: A Danish Population-Based Cohort Study. D. E. Schendel*[1], M. Overgaard[1], J. Christensen[1], L. Hjort[2], M. Vestergaard[1] and E. T. Parner[1], (1)*Aarhus University*, (2)*Aarhus University Hospital*

Background: Previous studies consistently report elevated mortality in persons with autism compared to the general population, but these findings are limited to older cohorts, small sample sizes or lack of recent follow-up. Mortality patterns have not been investigated in large, population-based birth cohorts that reflect the recent dramatic autism prevalence increase and with follow-up to the present time.

Objectives: Conduct a population-based longitudinal cohort analysis of mortality in individuals diagnosed with autism spectrum disorders (ASD) born from 1980 and followed through 2012, considering age, sex, ASD diagnosis, and pre- and perinatal factors.

Methods: The study cohort was comprised of all Danish births from 1980 through 2010 (N=1,934,672 births) identified in the Danish Medical Birth and Central Person Registers and study information for each cohort member was obtained through multiple national health registry linkages of individual-level data via a unique personal identifier. ASD and select other developmental outcome diagnoses in the child and parent psychiatric history diagnoses were obtained from the Danish Psychiatric Central Research Register; medical comorbidity diagnoses were obtained from the Danish National Patient Register; perinatal and birth information were obtained from the Danish Medical Birth Register; family demographics and mortality information were obtained from the Danish Central Person Register; cause of death was obtained from the Cause of Death Register. Mortality curves were derived using Kaplan-Meier methods. Hazard ratios of the relative risk of death in ASD versus non-ASD were estimated using Cox regression methods.

Results: By the end of follow-up (31 December 2012), 18,380 cohort children (1%) were diagnosed with ASD and 5187 (0.3%) were diagnosed with childhood autism, specifically. Fifty-eight deaths occurred in persons diagnosed with ASD, 15 deaths in persons with childhood autism. The relative risk of death was generally 2-fold higher or more in persons with ASD than non-ASD overall, and by sex, age, and perinatal or parent characteristics. Cause of death will also be reported.

Conclusions: Compared to their birth counterparts without ASD, persons born since 1980 with ASD are at increasing risk of death beginning in youth through early adulthood overall and the elevated risk is evident across a number of individual and parent characteristics present at birth. Understanding the contributions of long-term comorbidity on mortality risk is essential to guiding lifelong health care provision for individuals with ASD.

**121.115 115** Angiogenesis Drives Neurogenesis: Fetal-Placental Vascular Network Structure in a Population Based Cohort of ASD and Matched Controls. T. Girardi*[1], C. M. Salafia[1], C. Platt[2], D. P. Misra[3], R. Shah[4] and G. Merz[1], (1)*Institute for Basic Research*, (2)*University of Bristol Hospitals*, (3)*Wayne State University*, (4)*Placental Analytics*

Background: The placenta is a fetal organ that is reflective of the effect of fetal genes, and is also the direct interface with the maternal environment. It has a branched vascular structure that grows across gestation. There is evidence that angiogenesis drives neurogenesis, and that measures of the branched network structure of vascular beds may inform on neuroanatomy or connectivity.

Objectives: To determine whether placental chorionic surface vascular features are measurably different in children with autism or at high risk for autism and its spectrum disorders (ASD).

Methods: The Avon Longitudinal Study of Parents And Children (ALSPAC) recruited mothers delivering over a one year period 1991-1992. Followup was performed to diagnose autism/ASD. All children with ASD who retained placentas, and 3 controls per case were selected for this nested case control study. The placental chorionic surface was photographed. The surface vasculature was traced from the digital images by a dedicated team. Tracings were reviewed by one observer before analysis by a computer algorithm that extracted counts, lengths and distances between structures, branching angles and a measure of tortuosity. Data were analyzed in SPSS 20.0.

Results: There was a bimodal distribution of vascular branch point numbers in ALSPAC ASD cases, with the majority of ASD cases with reduced numbers and 6 cases with strikingly increased vascular branching, greater than 1 standard deviation above the mean expected for normal (ALSPAC control). Excluding the 6 outliers, there are striking differences in the placental chorionic surface arterial networks, with similar but generally smaller effects seen in the venous networks, including total reduction in the number of branch generations (although not in a change in the number of vessels originating off the umbilical cord), a reduction of 42% in vascular branch points, reduced total vascular surface length and decreased placental chorionic surface vessel extension to the perimeter, and altered branching angles (all p,0.05). There was no gender distinction; small sample sizes for female ALSPAC ASD cases limits the power of significance tests.

Conclusions: These data point to a difference in network structure of a key vasculature laid down in the fetal placenta contemporaneous to the evolution of fetal vasculature in the central nervous system. Placentas, most commonly discarded as medical waste, present an excellent opportunity to develop a panel of perinatal biomarkers for ASD risk assessment and may inform on the causal chain leading to ASD. We speculate that the observed bimodality reflects heterogeneity in ASD diagnosis in the 1990's compared with contemporary practice, as Rett's Syndrome and Fragile X Syndrome were not distinguished from ASD proper at that time.

**121.116 116** Changes in Psychiatrist Diagnoses of Autism and Other Mental Health Conditions in Israel Between 2003 and 2012. M. Davidovitch*[1], V. Sima[2], V. Shalev[2], G. Chodick[2] and L. Sigler[2], (1)*Maccabi Healthcare Services*, (2)*Maccabi Heathcare Services*

Background:

The dramatic increase in autism spectrum disorder (ASD) prevalence has been attributed to the broadening of diagnostic criteria, greater awareness, improved case finding methods, and the development of services for children with ASD. Diagnostic substitution has also been suggested as a reason for this increase, with several studies pointing to an increase in the diagnosis of ASD and a decrease in the diagnoses of intellectual disabilities, and other language and developmental disorders. However, to our knowledge, no studies have examined whether shifts in psychiatric diagnoses could contribute to the rise in ASD prevalence.

Objectives:

To describe the changes in diagnoses of autism and mental health disorders in children in Israel between 2003 and 2012, using data from psychiatrists in Maccabi Healthcare Services (MHS), a large healthcare organization in Israel.

Methods:

A search of the MHS computerized databases was conducted for all diagnoses given to children (up to the age of 18) by psychiatrists from 2003 to 2012. Diagnoses were grouped by year and

divided into ten broad categories, such as ASD, anxiety, and phobia. If a child received a diagnosis that fell into multiple categories, the diagnosis was listed in all relevant categories. However, if a child received the same type of diagnosis twice or more in a single year, the diagnosis was listed only once. The relative percentage change was calculated and chi square analysis was performed.

Results:

The total number of children diagnosed by psychiatrists in MHS increased from 1499 children in 2003 to 7327 in 2012. ASD accounted for 6.1% of all diagnoses in 2003, compared to 10.4% in 2012, representing a relative percentage increase of 69.2% ($p<0.001$). Statistically significant ($p<0.01$) relative increases between 2003 and 2012 were also found for behavior problems (60.7%), anxiety (58.6%) and ADHD (38.4%). A significant ($p<0.001$) decrease in the relative percentage between the same years was found for psychosis (58.5%), schizophrenia (40.8%) and depression (35.4%). Non-significant changes were found for phobia, obsessive compulsive disorder and bipolar diagnoses.

Conclusions:

Results indicate a substantial shift in psychiatric case mix among children (up to the age of 18) between 2003 and 2012 in one of Israel's largest healthcare organizations. ASD accounts for a growing proportion of all cases diagnosed by psychiatrists. While there was a relative increase also in behavior problems, anxiety and ADHD, there was a relative decrease in psychosis, schizophrenia, and depression. This shift may reflect psychiatric diagnosis substitution over time with an increasing number of children receiving an ASD diagnosis instead of other psychiatric diagnoses. Possible explanations for the shift in psychiatric case mix include increased awareness as well as a significant increase in services provided to children and adolescents with ASD.

**121.117 117** Concordance Between DSM-5 ASD Criteria and Community ASD Identification Under DSM-IV-TR in a Population-Based Study. M. J. Maenner*[1], C. Arneson[2], L. A. Carpenter[3], R. S. Kirby[4], C. E. Rice[1], L. A. Schieve[1], K. Van Naarden Braun[1], L. D. Wiggins[1], W. Zahorodny[5] and M. S. Durkin[2], (1)*Centers for Disease Control and Prevention*, (2)*University of Wisconsin-Madison*, (3)*Medical University of South Carolina*, (4)*University of South Florida*, (5)*Rutgers New Jersey Medical School*

Background: The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (*DSM-5*), published in 2013, included revised diagnostic criteria for autism spectrum disorder (ASD). Studies using clinical research samples have shown that some children who met ASD criteria based on *DSM-IV-TR* will not meet *DSM-5*ASD criteria, raising concerns about individuals "losing" their ASD diagnosis or no longer qualifying for certain services.

Objectives: To examine the relationship between ASD identification by community professionals and having documented symptoms consistent with *DSM-IV-TR* or *DSM-5*ASD criteria.

Methods: The Autism and Developmental Disabilities Monitoring (ADDM) Network performed population-based ASD surveillance for 8-year-old children living in 14 US communities in 2006 and 2008, using information abstracted from health or education records. Children's records were abstracted for clinician review if they contained diagnostic statements or behavioral symptoms suggestive of ASD. Trained clinicians systematically coded the information corresponding to the behavioral diagnostic criteria for Autistic Disorder, Asperger's Disorder, or Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), based on the *DSM-IV-TR*. Clinicians also noted when a child already had an ASD diagnosis or autism classification for special education. We operationalized the *DSM-5* ASD criteria using behavioral symptoms collected from developmental evaluations. Among 12,277 children with abstracted information, 45% had documentation of ASD by a community professional. We calculated the concordance between community ASD identification and having symptoms consistent with *DSM-IV-TR* PDD-NOS or Autistic Disorder, and between community ASD identification and having symptoms consistent with *DSM-5*ASD.

Results: The overall percent concordances between community ASD identification and documented ASD behavioral criteria were 53.6% for any *DSM-IV-TR* ASD, 74.5% for *DSM-IV-TR* Autistic Disorder, 35.4% for *DSM-IV-TR* PDD-NOS or Asperger's Disorder (excluding children meeting criteria for Autistic Disorder), and 74.3% for *DSM-5* ASD. Similarly, the percent of children

identified with ASD varied depending on the ASD criteria met: 49.4% of 10,753 children with documented behaviors indicating any *DSM-IV-TR* ASD; 67.7% of 6,908 children with documented behaviors indicating *DSM-IV-TR* Autistic Disorder, 16.6% of 3,845 children with documented behaviors indicating *DSM-IV-TR* PDD-NOS or Asperger's Disorder (excluding those meeting Autistic Disorder), and 68.7% of 4,453 children with documented behaviors indicating *DSM-5*ASD.

Conclusions: The *DSM-5* ASD criteria showed higher concordance with community ASD identification practices, suggesting that the *DSM-5* ASD criteria may, on the whole, better reflect current ASD identification practices in community settings than the *DSM-IV-TR* criteria. The lower concordance among those meeting *DSM-IV-TR* PDD-NOS criteria is consistent with previous clinical studies suggesting that more children meet the minimum symptom threshold for PDD-NOS than clinically appropriate. Despite the higher overall concordance, fewer children met *DSM-5* ASD criteria than the *DSM-IV-TR* criteria. Because the data collected for this study preceded the development of the *DSM-5*, additional studies are needed to monitor how community providers adopt the new ASD criteria.

**121.118 118** Development of a Novel Protocol for Characterizing Dysmorphology to Enhance the Phenotypic Classification of Autism Spectrum Disorders. S. K. Shapira*[1], L. H. Tian[1], A. S. Aylsworth[2], E. R. Elias[3], J. E. Hoover-Fong[4], N. J. Meeks[3], M. C. Souders[5], A. C. H. Tsai[3], E. H. Zackai[5], A. A. Alexander[1] and L. A. Schieve[1], (1)*Centers for Disease Control and Prevention*, (2)*UNC School of Medicine*, (3)*University of Colorado School of Medicine*, (4)*Johns Hopkins University*, (5)*The Children's Hospital of Philadelphia*

Background: Pediatric dysmorphology evaluations assess children for physical features that occur rarely in the general population. For example, short stature, protruding ears, and webbed toes are well-established dysmorphic features. Children with multiple dysmorphic features are more likely to have an underlying genetic condition or teratogenic exposure that affected the typical developmental process. In children with autism spectrum disorders (ASDs), the presence of multiple dysmorphic features might identify a distinctive ASD phenotype and serve as a potential marker for understanding cause and prognosis.

Objectives: To develop a quantitative method that defines criteria for classifying children as Dysmorphic in a case-control study of ASD, and to apply these criteria to determine if the proportion classified as Dysmorphic differs between children with and without ASDs.

Methods: This analysis included children enrolled in the Study to Explore Early Development (SEED), a multisite population-based case-control study of children aged 2-5 years with ASD (n=145) and two control groups, one drawn from the general population (POP, n=129) and one with non-ASD developmental problems (DD; n=90). Study participants received a physical examination including basic anthropometry and standardized body region photographs. Seven clinical geneticists were each assigned a body region—Head/Hair/Face/Neck, Ears, Eyes/Eyebrows, Nose/Philtrum, Mouth/Lips/Teeth, Hands/Feet, Growth/Skin—for which they conducted on every child a standardized dysmorphology review of potential dysmorphic features within just that body region. Each feature was scored: 0=normal/absent; 1=possible/questionable; 2=mild; 3=moderate; 4=severe. Geneticists were blinded to each child's study group assignment. For each reviewed feature, the scores that occurred in ≤5% of POP children (e.g., 4 only; 3 and 4 together; 2, 3, and 4 together) were designated as dysmorphic. To obtain a total dysmorphology score, the number of features (across body regions) designated as dysmorphic was divided by the number of all features scored for the child. The total dysmorphology scores for POP children were fit to the log normal distribution to delineate dysmorphology classifications: <90th percentile=Non-dysmorphic; ≥90th and <95th percentile=Equivocal; ≥95th percentile=Dysmorphic. Based on each feature's definition of dysmorphic in the POP children, total dysmorphology scores were similarly calculated for ASD and DD children and the proportions within each dysmorphology classification (based on the distribution for POP children) were compared between groups by chi-squared or Fisher's exact tests.

Results: These preliminary analyses included only non-Hispanic white children. Significantly higher proportions of children with ASD or DD were classified as Dysmorphic, compared with POP children ($\chi2=14.14$, $p=0.0008$ and $\chi2=10.99$,

p=0.0041, respectively). When children with known chromosome anomalies or genetic syndromes were removed from each group, the significant differences in dysmorphology classifications persisted between POP children and the other two groups. Within each group there was no significant difference in dysmorphology classification between boys and girls. Future analyses will evaluate racial/ethnic differences among ~1100 children in SEED.

Conclusions: More ASD group children met criteria to be classified as Dysmorphic than children in the POP group. This novel protocol defines a quantitative dysmorphology classification and identifies categories of Dysmorphic and Non-dysmorphic children with ASDs. These children can be further assessed according to etiologic risk factors.

**121.119 119** Environmental Exposure Measured in Deciduous Teeth As Potential Biomarkers of ASD Risk. R. F. Palmer*[1], L. Heilbrun[2], D. Camann[3], S. Schultz[2] and C. Miller[2], (1)*University of Texas Health Science Center San Antonio*, (2)*University of Texas Health Science Center*, (3)*Southwest Research Institute*

Background: Gene/environment (G x E) interactions are now widely regarded as the most probable explanation for idiopathic autism. However, in order for G x E interactions to be evaluated, valid biomarkers of exposure must be identified. Indeed, the largest roadblock to investigating adverse environmental exposures has been identifying valid biomarkers of exposures that occur during critical developmental periods. We have made significant progress this year with our discovery that semivolatile organic chemicals can be measured in shed deciduous teeth. We present further validation that chemicals measured in teeth can be used as biomarkers of early developmental exposure.

Objectives: The purpose of our study was to determine if maternal retrospective reports about their children's exposures to various chemicals would correspond to the chemical concentrations found in the child's deciduous teeth.

Methods: Seventy-one (71) deciduous teeth were chosen from our tooth repository consisting of 928 children's deciduous teeth. These 71 teeth were to be analyzed for acetaminophen, DEET, pesticides, phthalates (plastics), and fatty acids. The selection of these teeth was determined by examination of survey responses provided by the mothers. We chose teeth based on both high and low self-reported exposures to determine if there would be a correspondence with chemicals measured in their children's teeth. All children were recruited from the Interactive Autism Network (IAN) with diagnoses of autism. Electrospray ionization liquid chromatography tandem mass spectrometry (LC/MS/MS) in multiple reaction monitoring mode was used to determine the concentrations of targeted chemicals in the pulverized tooth samples.

Results: There was a 44% detection rate for acetaminophen, a 75% detection rate for insect repellant (DEET), a 13% detection rate for insecticide metabolites and from 40-100% detection rate across 4 phthalate metabolites. Among those self-reporting the highest cumulative use of acetaminophen, 53.5 percent (n = 23/43) had detectable amounts of acetaminophen in teeth compared to 28.6 percent (n = 8/28) detection in the lower exposure group (Fisher exact test = p <.051). DEET was regressed on self-reported repellant use yielding a .41 standardized beta with an R-square of .16 after adjustment for parental age and child gender (p<.002). Chi-Square analysis shows that 90.9 percent of those in the highest self-reported exposure category had detectable amounts of DEET in teeth compared to 63.3 percent detection in the lowest self-reported exposure group (fisher exact test = p <.01). There was a significant association between self-reported fume/chemical exposure and measured tooth phthalate metabolites during the time frames of pregnancy and after child birth (p<.05). There was no significant difference between self-reported pesticide exposure and pesticides measured in teeth.

Conclusions: Consistent with our prior report in the Journal of Exposure Science (Camann et al, 2013), we have demonstrated that specific semi-volatile organic chemicals can be detected in deciduous teeth. The current results indicate that mothers self-report of their child's early exposure to acetaminophen, phthalates and DEET are consistent with measured amounts or detection in the child's deciduous tooth. This provides some validation that teeth may be used as viable biomarkers of exposure during this developmental timeframe.

**121.120 120** Extremely Preterm Born Children Are at Very High Risk for Developing Autism Spectrum Disorder. L. Verhaeghe* and H. Roeyers, *Ghent University*

Background:

Advances in neonatal and perinatal care have increased the survival rate of extremely preterm children, children born before 28 weeks of gestation. Although this is a positive evolution, follow-up studies have shown that these children are at an increased risk of developmental problems in various domains. Recent evidence also suggests a link between prematurity and autism spectrum disorder (ASD) (Johnson et al., 2010; Limperopoulos, 2009; Moore et al., 2012; Stephens et al., 2012). It appears that ASD is an under-recognized problem in this group of children.

Objectives:

Our study aims to investigate the prevalence of ASD in a cohort of extremely preterm children who are now in their early teens. Previous prevalence studies were predominantly based on screening instruments and did not include diagnostic confirmation. By using diagnostic instruments in addition to screening instruments to determine the prevalence of ASD, we want to provide a more reliable picture.

Methods:

We conducted a follow-up study of the EPIBEL children. EPIBEL is an acronym of a study investigating Extremely Preterm Infants in BELgium. Perinatal data of all the surviving children born between 22 and 26 completed weeks of gestation in a two-year period (January 1, 1999 to December 31, 2000) in Belgium were collected (Vanhaesebrouck et al., 2004). At 3 years of age, the cognitive, language and motor development of the 95 Flemish children was re-assessed by our research group (De Groote et al., 2007). This group was visited again between the ages of 11 and 13. In the first part of this study, parents were asked to complete the Social Communication Questionnaire (SCQ; Rutter, Bailey & Lord, 2003) and the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005). In the second part, diagnostic evaluation of the children who already received a clinical diagnosis and of the positive screens included the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore & Risi, 1999). Parents are currently being interviewed with the Autism Diagnostic Interview – Revised (ADI-R; Rutter, Le Couteur & Lord, 2008).

Results:

Results suggest that the prevalence of ASD is very substantially higher in this group than in the general population. Of the participating children, 24.4% were clinically diagnosed with ASD. In addition, 13.3% of the children scored above the cut-off of the ADOS. Significant correlations with the ADOS severity score were found for birth weight, the 5 minute Apgar score and for the Mental and Psychomotor Developmental Indexes of the Bayley Scales of Infant Development (BSID-II; Bayley, 1993) at age three. Male gender was also significantly associated with being diagnosed with ASD.

Conclusions:

This study confirms findings of previous research which suggested an elevated rate of ASD in extremely preterm born children. In this Flemish cohort of children born before 26 completed weeks of gestation, the prevalence of ASD was found to be 37.8% after a screening procedure and a clinical diagnostic evaluation and/or a research evaluation with the ADOS. It is clear that extreme preterms are a high-risk group for developing ASD that deserves increased clinical and research attention.

**121.121 121** Focus Group Contributions to the Early Life Exposure Assessment Tool (ELEAT). M. C. Oliver*[1], R. J. Schmidt[2] and C. K. Walker[3], (1)*UC Davis MIND Institute*, (2)*University of California at Davis*, (3)*UC Davis*

Background: Accurate estimation of gestational exposure risk relies most commonly on maternal report of retrospective events, since acquisition and abstraction of more objective data from medical records is both expensive and labor-intensive. The ELEAT (Early Life Exposure Assessment Tool) has been created through an exhaustive examination of evidence along with extensive validation and reliability testing of candidate questions and is projected for widespread use as a survey of environmental risk during early neurodevelopmental periods.

Objectives: The aim of this study was to obtain stakeholder feedback on the ELEAT experience

and suggestions for its improvement. Discussion focused on question clarity and content and module length, formatting and mode of administration.

Methods: We conducted two-hour focus groups with mothers of children with ASD and/or typical development from different settings after receiving informed consent. Specific guidance was sought to hone questions and modules, determine the most logical question order, simplify formatting and shorten the instrument. The first group was composed of mothers of children with ASD who had undergone telephone administration of the ELEAT. Healthcare workers who had self-administered the survey and who worked at and received healthcare from local community clinics comprised the second group. The third group included women receiving reproductive care in the same clinic system who had no prior experience with the ELEAT. Groups were led by a professional facilitator experienced in exploring health and environmental topics. Another staff member recorded salient patterns and themes from the discussion onto visual media for the group to follow and revise during the session.

Results: Focus group participants averaged 32 years of age and had a mean of 4 children. There were 41% White, 17% Black, 5% Asian, and 17% each were multi-racial or unreported. Most participants were born in the U.S. (82%) and spoke English at home (88%). Thirty-five percent had technical/vocational training, and 11% were in each of the following groups: some high school, graduated high school, some college, completed college, and postgraduate education. Despite group differences, similar themes emerged. Participants agreed that the survey needed more gateway questions, streamlining of questions, lower literacy level and increased cultural sensitivity. Interestingly, they agreed that the survey should not be shortened and favored online self-administration.

Conclusions: Linking peri-gestational experiences to subsequent neurodevelopment requires careful attention to exposure assessment. The ELEAT has been modified in response to focus group concerns. More extensive use of gateway questions and streamlining of content reduced redundancy and increased user-friendliness. Lowering the literacy level should improve response accuracy in those with less education. Enhancing cultural sensitivity of the instrument will embrace diversity and foster an atmosphere in which the varied life experiences of parents are recognized and respected. The ELEAT provides evidence-based peri-gestational exposure assessment using questions that have been refined based on participant feedback. The current survey minimizes participant burden and maximizes collection of accurate data and can be used by divergent investigators and populations to study risk factors for neurodevelopmental disorders such as ASD.

**121.122 122** Influence of Family Demographic Factors on Social Communication Questionnaire (SCQ) Scores. E. Moody*[1], S. Rosenberg[2], L. C. Lee[3], M. D. Fallin[3], G. C. Windham[4], L. Wiggins[5], C. DiGuiseppi[6], L. A. Schieve[5], S. E. Levy[7], L. Blaskey[7] and L. M. Young[8], (1)*University of Colorado, Denver*, (2)*University of Colorado School of Medicine*, (3)*Johns Hopkins Bloomberg School of Public Health*, (4)*California Dept of Public Health*, (5)*Centers for Disease Control and Prevention*, (6)*University of Colorado - Denver*, (7)*Children's Hospital of Philadelphia*, (8)*U Penn*

Background: Screeners for autism spectrum disorders (ASDs) are important for determining ASD risk in population-based studies. Consequently, identifying socio-economic status (SES) factors that affect the validity of an ASD screener can improve the accurate identification of autism-related behaviors and inform future screening efforts. The Social Communication Questionnaire (SCQ) is a parent report screener for ASD that has been widely used in epidemiological studies. It is unclear whether SES factors affect the performance of the SCQ, as studies have reported conflicting findings (Corsello et al, 2007; Tsai et al, 2012).

Objectives: To examine the impact of maternal race, ethnicity, language, education and family income on SCQ scores.

Methods: SCQ data were collected in the Study to Explore Early Development-Phase I (SEED I), a multi-site (California, Colorado, Georgia, Maryland, North Carolina and Pennsylvania) case-control study exploring the phenotypes and determinants of ASD. Participants aged 2-5 years were recruited through organizations providing ASD-related services and from randomly selected vital records. Participants were screened using the SCQ to determine ASD risk. Children were classified as ASD, non-ASD developmental disability (DD), or population-comparison (POP)

after screening and a clinical assessment for those with 11 or more points on the SCQ. Demographic data were collected in a standardized maternal interview. Separate linear regressions were run for children with final classification of ASD (n=667, SCQ mean = 17.2 ± 6.1), DD (n=990, SCQ mean = 7.2 ± 5.1) and POP (n=936, SCQ mean =4.3 ± 3.2). In all models, family income (<10K, 10-30K, 30-50K, 50-70K, 70-90K, 90-110K, >110K), maternal education (less than high school, high school, some college/trade, bachelor degree or advanced degree), maternal race (White, Black, Asian, Native American/Native Alaskan/Native Hawaiian/Pacific Islander, Multi-racial), ethnicity (Hispanic, Non-Hispanic) and language in the home (Spanish or English) were regressed on total SCQ score (range 0-35).

Results: This work reports preliminary results for our study sample. Higher SCQ scores were predicted in the ASD group for lower family income ($\beta$=-.60, $p$<0.001), in the DD group for lower family income ($\beta$ =-.70, $p$<0.001) and less maternal education ($\beta$ =-.90, $p$<0.001), and in the POP group for lower family income ($\beta$ =-.32, $p$<0.001) and less maternal education ($\beta$ =-.62, $p$<0.001). Maternal race and ethnicity and language spoken in the home did not have a significant influence on SCQ scores in any study group. Collinearity was not a concern in any of the models.

Conclusions: Our results indicate that SCQ scores are influenced by family demographics, particularly family income and maternal education. Lower family income predicted higher SCQ scores for children in all three SEED study groups. Moreover, less maternal education predicted higher SCQ scores in the DD and POP comparison groups. These results indicate that family income and maternal education appear to be important considerations when interpreting SCQ scores; future revisions of the SCQ should take into account the influence of these demographic variables. Future analyses could consider the sensitivity, specificity, positive predictive value, and negative predictive value of the SCQ when stratified by demographic variables.

**121.123 123** Integration of Environmental Variables into Autism Genetic Repository Data. H. E. Volk*[1], A. Kalkbrenner[2], N. L. Lee[3], F. Lurmann[4], H. Minor[4] and G. C. Windham[5], (1)*University of Southern California*, (2)*University of Wisconsin-Milwaukee*, (3)*Drexel University School of Public Health*, (4)*Sonoma Technology, Inc.*, (5)*California Dept of Public Health*

Background: Genetic repositories for research on autism spectrum disorders (ASD) often contain data on well-phenotyped individuals and have biospecimen resources, yet little information on environmental risk factors. Having detailed data in all these domains would allow the investigation of main effects of environmental exposures or gene-environment interactions.

Objectives: We assessed the ability to determine place of residence as an approach to characterizing environmental exposures, specifically evaluating two methods for gathering residential addresses for participants in the Autism Genetics Resource Exchange (AGRE): 1) Re-contact using a self-administered web-based questionnaire, and 2) Use of a publicly-available computerized address search engine. In this study, we focused on prenatal and early life exposures to air pollutants for children in AGRE.

Methods: AGRE families with at least one child born 1994-2007 were eligible for our study. Since AGRE is composed of children with ASD and their siblings, parents/guardians were contacted via email or postal letter and asked to complete a residential history online. Separately, study contact (parent/guardian) information was used to conduct a computerized search of up to 10 historical addresses using LexisNexis. All collected addresses were filtered based on dates of residences to identify those corresponding to the nine months before birth or two years after birth for eligible children. Addresses were geo-coded and air quality data was assigned using the EPA's AIRNOW monitoring network and roadway distance assigned using roadway geometry.

Results: A total of 1,373 families (4,508 children) from AGRE were eligible for our study. All families were included in both address-finding methods. The online residential history form was completed for 716 children from 305 families, reflecting only a 22% family participation rate. LexisNexis search results were returned for 96% of families, providing at least one historical address for 3,119 children (69%). We combined these two ascertainment methods to compile the most complete resource possible, and filtered for addresses pertaining to the exposure time window of interest. This resulted in assignment of at least

one residential address for 2,550 children (57%) during the prenatal and two-years postnatal period. Of these children, roadway distance was assigned for 2,343 (92%). Air quality assignments based on EPA monitor data were made for 43-83% of residential locations, resulting in sample sizes up to 1,948 children (in the case of Particulate Matter) with both air pollutant and roadway distance data for future analyses.

Conclusions: The study of geographically determined environmental exposures is possible for biorepository participants using ancillary resources, but requires access to personally identifiable data to allow the most complete address tracing. The rich genetic, phenotypic, and family information, with new environmental data on hundreds of children, comprise a valuable resource for future studies, although careful analysis of subject non-participation or non-inclusion is needed.

**121.124 124** Maternal Education Predicts Early ASD Diagnosis in Black and White Toddlers with Higher Cognitive Functioning. S. Fernandez-Carriba*[1], C. A. Saulnier[1], J. Berman[1], B. Davis[1], G. Kneeland[1] and A. Klin[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

Background: Recent studies on disparities in ASD across racial and ethnic groups highlight the role of cognition as an essential modulator variable. Magnusson et al. (2012) reported higher rates of low-functioning ASD for minorities in Sweden, and Durkin et al. (2010) found a positive association between socioeconomic status and ASD in all US ethnic groups, but no association when ASD presented with cognitive delays. ASD has also been found to be less prevalent but more severe in minorities in the US (Mandell et al., 2009).

Objectives: This study explores level of functioning in newly diagnosed toddlers with ASD across two different sociodemographic variables: race and socioeconomic status.

Methods: 131 toddlers ages 10 to 30 months (Mean=22.13, SD=4.32) were recruited from a clinically-referred sample; 100 participants were white (52 ASD; 26 DD; 22 TYP; 25 females) and 31 participants were black (17 ASD; 12 DD; 2 TYP; 7 females). Evaluations included the *Autism Diagnostic Observation Schedule, Toddler Module*, the *Vineland Adaptive Behavior Scales, Second Edition,* and the *Mullen Scales of Early Learning*. Race was computed by self-identification, and SES by level of maternal education (college degree or more and less than college degree). Mullen derived IQ scores were grouped as higher or lower than 70 (High IQ; Low IQ).

Results: Results showed no significant difference in age of diagnosis between racial groups. Chi-Square analyses revealed no significant effects of race by diagnosis, race by maternal education, or race by IQ, but did reveal a significant effect for maternal education by diagnosis, with 46% of mothers of children with ASD having a college degree or higher compared to 31% of the DD sample [$\square\chi^2(2)=10.65$; $p<.01$]. Age of diagnosis in children with ASD with High Verbal IQ was significantly lower if their mothers' education was a college degree or higher [M=16.86m, SD=1.70] vs. some college or less [M=23.29m, SD=6.01, t(12)=12.62, p<.05). Similarly, children with High Nonverbal IQ were diagnosed with ASD earlier if their mothers had a college degree or higher [M=21.00m, SD=4.71] compared to less than college [M=24.10m, SD=2.43, t(43)=7.42, p<.05]. Conversely, maternal education did not predict any differences in age of diagnosis for children with ASD with Low IQ. For the DD samples of both Low and High IQ, there were no significant effects of maternal education on age of diagnosis.

Conclusions: In a biracial sample of clinically-referred toddlers that is relatively homogeneous in terms of maternal education and cognitive functioning, higher maternal education predicts earlier diagnosis of ASD in cognitively intact children, but not those with delays. Maternal education is not associated with earlier diagnosis of DD. These results corroborate Durkin et al. (2010), showing less ethnic differences in families with higher SES, and a greater SES gradient in children without cognitive delays (regardless of race). Given that ASD unfolds with development, future studies should focus on young children that are diagnosed early in order to characterize the true status of cognitive functioning in autism and disentangle its interaction with sociodemographic factors.

**121.125 125** Minneapolis Somali Autism Prevalence. A. S. Hewitt*[1], J. Punyko[2], K. Hamre[1], A. N. Esler[1] and J. Reichle[1],

(1)*University of Minnesota*, (2)*Minnesota Department of Health*

Background: The national prevalence rate in the United States for ASDs based on 2008 data is one in 88 (CDC 2102). The prevalence rate in Minnesota for the calendar year 2008 is not known because surveillance was not in place. In 2008, Somali advocates in Minneapolis expressed concerns to the Minnesota Department of Health about more Somali children, ages 3 through 5, enrolled in preschool special education programs for ASD as compared to the overall percentage of Somali children enrolled in the city's public schools. That study found: the proportion of Somali children ages 3 and 4 who participated in the ECSE ASD program was higher than for children of other races or ethnic backgrounds; the proportion of preschool Asian and Native American children who participated in the ECSE ASD programs was strikingly low, and differences in participation rates between preschool Somali children and preschool children of other races and ethnic backgrounds decreased substantially over the three school years studied. This presentation will share the process and findings of a study funded by the CDC, NIH and Autism Speaks that engaged the Somali community in investigating the prevalence of autism in 7 – 9 year olds in calendar year 2010 using school and clinic records. Examples of community engagement, training and targeted dissemination strategies will be shared. Additionally the overall and Somali prevalence findings from the study will be shared.

Objectives:

a) Present findings from a prevalence study of Autism Spectrum Disorders (ASD) in the Minneapolis, MN Somali population; b) Discuss ways to engage immigrant communities c) Share targeted dissemination strategies and d) Discuss lessons learned. Presenters will discuss the importance and benefits of community involvement, and the challenges to engagement within a prescribed research methodology.

Methods:

This study replicated and augmented the CDC Autism and Developmental Disabilities Monitoring Network (ADDM).While not an ADDM Network site, rising concerns about the prevalence of ASD in Minnesota, and in particular among the Somali population, were the impetus for this study. This study sought to understand the characteristics of children with ASD, and to highlight the impact of ASDs on communities and families.

While the ADDM Network provides information on ASD prevalence, the Minnesota project sought to understand prevalence with specific inquiry into the Somali population. The community has a strong advocacy presence, and involving representatives from this community and from key provider organizations was a critical component of the project. Engagement occurred in the planning, implementation, and dissemination stages. Direct community involvement and engagement in project activities is distinct from typical ADDM Network sites, and presenters will discuss the implications implementing the study in this way.

Results:

The rsults are not yet public and will be released in November of 2013 (but not in time to include in this abstract). Results will be presented that identify prevalence, case ascertainment, co-occuring conditions and severity of symptoms (for Somali, non Somali and white only).

Conclusions:

Implications of the findings related to policy, service access and utilization, early identification and further research will be discussed.

**121.126 126** Neonatal Cytokines and Chemokines and Risk of Autism Spectrum Disorder: The Early Markers for Autism (EMA) Study. O. Zerbo*[1], C. K. Yoshida[1], J. K. Grether[2], P. Ashwood[3], R. L. Hansen[4], J. Van de Water[3] and L. A. Croen[5], (1)*Kaiser Permanente Division of Research*, (2)*California Dept of Public Health*, (3)*UC Davis*, (4)*M.I.N.D. Institute/UCDavis*, (5)*Kaiser Permanente Northern California*

Background: Markers of inflammation and/or infection have been associated with autism spectrum disorders (ASD) but prior studies have largely relied on specimens taken after clinical diagnosis. Research on biologic markers early in neurodevelopment is required to evaluate possible causal pathways and screening profiles. Cytokines and chemokines are immune signaling molecules and growth factors that can also affect neuronal development.

Objectives: To investigate levels of cytokines/chemokines in newborn blood

specimens as possible early biologic markers of dysregulation for autism.

Methods: We conducted a population-based case-control study nested within the cohort of infants born from July 2000 – September 2001 to women who participated in the prenatal screening program in Orange County, California. Cases (n = 84) were all children receiving services for autism spectrum disorder (ASD) at the Regional Center of Orange County. Two comparison groups from the same study population were included: children with developmental delay (DD, n = 49) receiving services at the same regional center, and children not receiving services for developmental disabilities, randomly sampled from the California birth certificate files and frequency-matched to autism cases on sex, birth year, and birth month (GP, n =159).

Neonatal cytokine and chemokine concentrations were measured in archived newborn screening bloodspots maintained by the California Department of Public Health using a commercially available multiplex bead-based kit (BioSource Human Bead Kit; Invitrogen, Carlsbad, CA, USA). The following cytokines and chemokines were measured: IFN-γ, IL-2, IL-4, IL-5, IL-6, IL-1β, IL-8, IL-10, IL-12p40, tumor necrosis factor alpha (TNF-α), granulocyte macrophage colony-stimulating factor (GM-CSF), IFN-γ-induced protein 10 (IP-10), MCP-1, Macrophage Inflammatory Protein-1alpha and 1beta (MIP-1α ,MIP-1β), RANTES and EOTAXIN. The assays were carried out in accordance with the protocols provided by the manufacturer. We compared levels of cytokines/ chemokines among ASD vs. GP and DD vs. GP using crude and multivariate logistic regression analyses.

Results: Cytokines were not detected in the vast majority of newborn samples regardless of case or control status. However, ASD cases were more likely than GP controls in a multivariate analysis to have levels of MCP-1 above the 90th percentile (odds ratio (OR) = 3.72, 95% confidence interval (CI) 1.56 – 8.86). They were significantly less likely to have levels of RANTES (OR = 0.36, 95% CI 0.15 – 0.85) above the 10$^{th}$percentile of the GP controls. The DD group was also less likely to have levels of RANTES (OR = 0.31, 95% CI 0.11 – 0.87) and MIP-1α (OR = 0.33, 95% CI 0.12 – 0.91) above the 10th percentile of the GP controls.

Conclusions: Measurement of newborn levels of the chemokines MCP-1, RANTES and MIP-1α might be useful in understanding mechanisms of early abnormal neurodevelopment. Each of these chemokines plays a role in neuron development. While often associated with inflammation, sufficient levels of these chemokines are needed for healthy neuronal migration. Therefore, changes in levels during critical windows of development could alter neurodevelopmental outcome.

**121.127 127** Parental Age Effects and Autism Spectrum Disorder: Exploring the De Novo Mutation Hypothesis in Affected Families. G. C. Windham*[1], M. Anderson[2], T. J. Hoffmann[3], L. A. Croen[4], J. K. Grether[5] and N. Risch[6], (1)*California Department of Public Health*, (2)*Impact Assessment, Inc.*, (3)*UCSF Institute for Human Genetics*, (4)*Kaiser Permanente Northern California*, (5)*California Dept of Public Health*, (6)*University of California, San Francisco*

Background: Epidemiologic studies have consistently shown an increased risk for autism spectrum disorder (ASD) with advanced parental age, with many showing independent associations of maternal and paternal age. Recent genetic studies have pointed towards de novo mutations as possibly associated with risk of ASD, and also associated with advanced paternal age. The de novo mutation–advanced paternal age model of ASD would imply different expected patterns of paternal age in families with single (e.g. "de novo") versus multiple (greater genetic susceptibility) children with ASD.

Objectives: Examine whether paternal age is greater for affected children in simplex compared to multiplex families.

Methods: We examined this in a large collection of nuclear families containing two or more children, with at least one affected with ASD, derived from linking the electronic files of the California Department of Developmental Services to state birth certificates, and matching to siblings by parental information. A total of 11,859 families were studied with children born 1990-2003, including 11,190 simplex and 669 multiplex families (with 1,369 affected children). We compared mean paternal and maternal ages at the birth of affected children in simplex versus multiplex families, stratified by birth order and sib-ship size, also calculating strata-specific differences. An overall weighted average of differences was calculated by weighting each

strata difference by the inverse of its standard error. We also categorized age and calculated odds ratios (OR) for the likelihood of affected children being in multiplex vs. simplex families, adjusting for parental race and education as well as birth order and sib-ship size.

Results: None of the mean paternal ages by birth order-sibship size strata were significantly increased in simplex vs. multiplex families. Rather, paternal and maternal age tended to be older for those with affected children in multiplex compared to simplex families (overall: paternal, 32.5 vs. 31.9 years; maternal, 29.6 vs. 29.0 years, respectively, or strata-weighted average differences of 0.82 years for fathers and 0.88 years for mothers). Similarly, the proportion of cases from multiplex families (10.9% overall) generally increased with increasing parental age category. In adjusted logistic regression models, we found a pattern of higher risk of being from a multiplex vs. simplex family with older paternal age (OR=1.34; 95% CI 1.00-1.81 for ≥ 45y). The pattern was attenuated, but did not change direction, when examining paternal age at birth of first affected child only. The risk also somewhat increased with maternal age (adjusted OR=1.27, 95% CI 0.89-1.81 at ≥ 40y); including both parents in the model did not change the direction of paternal age associations. The patterns did not vary greatly by gender of the affected child.

Conclusions: The results from this study, based on the largest set of simplex and multiplex families assembled for analysis, do not support the hypothesis that the observed paternal age effect for ASD is due to de novo mutation as it was not greater in simplex families, examined by two different analytic approaches. An alternative model that explains both advanced maternal and paternal age should be sought.

**121.128 128** Parental Age and the Risk of Autism Spectrum Disorders – Findings from a Swedish Population-Based Cohort. S. Idring*[1], C. Magnusson[1], M. Lundberg[1], D. Rai[2], A. Svensson[1], C. Dalman[1], H. Karlsson[1], M. Ek[1] and B. K. Lee[3], (1)*Karolinska Institutet*, (2)*University of Bristol*, (3)*Drexel University School of Public Health*

Background: There is evidence that both maternal and paternal age are independently associated with increased risk for ASD. However, as it is increasingly apparent that ASD represent a heterogeneous group of disorders with potentially different etiologies, there is a need of studies of parental age effects on different phenotypes of ASD. To date, few studies have examined whether associations between parental age and ASD differ by intellectual disability (ID), which is the most frequent co-occurring condition in ASD and associated with poor outcome.

Moreover, the majority of previous studies of parental age and ASD have used categorical parameterizations of parental age. While categorical parameterizations allow for easily interpretable results, continuous parameterizations of age allow for flexible, non-linear associations that are frequently less biased and more efficient. We used penalized cubic regression smoothing splines implemented in generalized additive models (GAMs) to model the independent, and mutually dependent associations of maternal and paternal age and risk of offspring ASD, subtyped by co-morbid ID, using a large, Swedish total-population-based cohort. We estimated whether parental age effects were affected by adjustment for known and potential confounders, and tested whether our results were robust to influences from extreme parental age, or a genetic condition associated with advanced maternal age and ASD.

Objectives: The objectives of this study were to examine the independent and dependent associations of maternal and paternal age and risk of offspring autism spectrum disorders (ASD), with and without intellectual disability (ID).

Methods: The sample consisted of 417,303 Swedish children born 1984-2003. ASD case status (N=4746) was ascertained using national and regional registers. Smoothing splines in generalized additive models accounting for interactions of maternal and paternal were used to estimate associations of parental age with ASD.

Results: While advancing parental age increased the risk of child ASD, maternal age effects were non-linear while paternal age effects were linear. Compared to mothers at the median age 29 years, those ≤29 had similar risk, while risk increased after age 30, with an OR of 1.76 (95% CI: 1.63-1.90) at ages 40-45. For fathers, compared to the median age 32 years, the OR for ages 55-59 was 1.39 (1.29-1.50). In analyses stratified by co-parental age, increased risk due to advancing paternal age was evident only in mothers ≤ 35 years. In contrast, maternal age increased risk

regardless of paternal age. Advancing parental age was more strongly associated with ASD with ID, compared to without ID.

Conclusions: We confirm prior findings that advancing parental age increases risk of ASD in a manner dependent on co-parental age. While recent attention has emphasized the effects of older fathers on ASD risk, an increase of *N* years in maternal age has greater implications for ASD risk than a similar increase in paternal age.

**121.129 129** Parental Concerns, Socioeconomic Status and the Risk of Autism Spectrum Conditions in a Population-Based Study. X. Sun*, C. Allison, B. Auyeung, S. Baron-Cohen and C. Brayne, *University of Cambridge*

Background: Epidemiological studies consistently find an association between Autism Spectrum Conditions (ASC) and high socioeconomic status (SES) in families. We hypothesized that parents with high SES might have more concerns about their children with ASC. So far, limited research has investigated the association between parental concern, socioeconomic status and the risk of having ASC.

Objectives: To investigate whether higher levels of parental concern about autistic symptoms predict higher risk of meeting ASC criteria; To investigate whether the SES of parents plays a role in any association between parental concern and risk of having ASC.

Methods: A total number of 11,635 screening packs were distributed to 5-10 year-old children in 136 schools in Cambridgeshire. Parental concern was examined by using the Social Difficulty Questionnaire (SDQ). The socioeconomic status of parents was generated using the self-coded National Statistics Socio-economic Classification (NS-SEC). The ASC status of children was investigated through assessments using ADOS and ADI-R and clinical diagnosis. The variables for investigating associations and possible confounders were extracted for analysis, including parental concern question score, SES, age of the child, sex, maternal age at birth, father's age at birth, maternal age at leaving education, father's age at leaving education, birth order and the number of children in the family. The associations between levels of parental concern (none/minor/strong) and SES, as well as the other variables were tested (Chi-squared). The association between parental concern, SES and the risk of ASC was examined by adjusting all the other variables in the model using unconditional logistic regression.

Results: The SES, age of the child, sex and maternal age at leaving education were associated with parental concern. Parents with higher SES reported higher levels of concern (*Chi-square*=11.8; $p$=0.02). However, a higher SES was not associated with the risk of having ASC ($p$=0.50). Sex was found to be associated with both parental concern and the risk of ASC, and both were included in the final model. After adjusting for potential confounders, the odds of children meeting ASC criteria whose parents had reported strong parental concern were 8.5 times (odds ratio: 8.5; 95%CI: 4.5, 16.2; $p$<0.001) the odds of children having ASC whose parents reported minor concern. No child met ASC criteria where parents expressed no concerns.

Conclusions: Parents with higher social class express more concerns than those from lower social classes. However, the concerns reported by parents in higher SES did not appear to be specific for ASC as there was no relationship between ASC and SES. Parental concern itself was strongly associated with a child meeting ASC criteria. The higher the degree of parental concern over their child in terms of emotions, concentration, behaviour or getting on with others, the more likely it is that the child will have ASC, independently of potential confounders. Conversely this study shows that where there is no parental concern expressed a child is extremely unlikely to meet diagnostic criteria. These findings should be of value in discussions related to which measures at what times are helpful in identifying children with ASC.

**121.130 130** Placental Features in ASD Compared to Controls: A Community Based Cohort in Brooklyn. K. Patel*[1], H. I. Collins[1], S. Mittal[2], R. Schubert[1], C. M. Salafia[2], P. Narula[1] and B. Zimmerman-Bier[3], (1)*New York Methodist Hospital*, (2)*Institute for Basic Research*, (3)*St Peters Univwersity Hospital*

Background: The prenatal environment is increasingly appreciated to conribute to ASD risk, but the precise mechanisms or causal pathways are unclear. The placenta is a fetal organ commonly discarded at birth but which is the fetal interface with the maternal environment and its growth is the reflection of fetal genetic regulation. Do placentas of children diagnosed with ASD at>2

years of age differ from developmentally normal controls? If angiogenesis drives neurogenesis, and placental angiogenesis drives villous arborization, is the ASD placenta structurally different? Does placental evidence of prenatal exposure to acute or chronic inflammation occur more commonly in ASD?

Objectives: To study the placental pathology, maternal diagnoses and newborn factors of all children followed at New York Methodist Hospital with ASD diagnosis and population based controls in a setting with universal placental pathology examination.

Methods: Billing codes were searched to identify all children with ASD diagnosis followed by either a pediatric neurologist or developmental pediatrician. Newborns matched for gender, birthweight (BW) and gestational age (GA) were also identified and maternal medical records, placental pathology report and newborn charts were reviewed. Data were analyzed in SPSS 20.0, with $p<0.05$ significant.

Results: 34 children with ASD (29 males and 5 females) and 124 controls had mean BW 3170 and 3328 g, GA 37.8 and 38.5 weeks. There was no difference in placental weight or the ratio of birth to placental weight. However, disk thickness differed significantly, with ASD placentas 10% thinner on average (2.56+ .44 v 2.81+ .54, $p=0.015$). There was no difference in chorionic plate surface area or ellipsivity of the disk. There was no association of labor induction or maternal fever with ASD case status. However, acute fetal inflammation of chorionic plate and chronic placental inflammation were each more common in ASD cases ($0.01>p<0.05$). Chronic placental inflammation was associated with reduced disk thickness at the $p=0.05$ level.

Conclusions: Placental disk thickness reflects the extent of branching villous arborization that creates the tissue interface between the mother's and the fetal bloodstreams. Villi are formed when vessels branch; reduced villous branching means reduced branching angiogenesis. Reduced disk thickness –implying reduced villous branching growth-- without a change in placental weight implies a difference in placental villous "composition". Given the evidence that angiogenesis drives neurogenesis, we propose that the placenta in ASD shows reduction in branching growth that may be paralleled by neuronal connectivity in the ASD brain. Prenatal exposure to inflammation has been suggested to underlie as many as 1/3 of ASD cases; we have preliminary evidence that placental measures of acute inflammation and chronic inflammation differ in ASD cases compared to population – based controls. Fetal inflammatory response was increased in ASD despite no association of ASD with maternal fever. Thus, these cases of prenatal exposure to acute inflammation were clinically silent. Chronic inflammation appears to be correlated with altered disk thickness; additional studies are needed to determine a potential link of inflammation and abnormal branching angiogenesis that could result in both our placental observations of abnormal villous "composition", and increased risk of ASD.

**121.131 131** Predictability of the Social Communication Questionnaire (SCQ) on Autism Diagnoses from a Community Study in Taiwan.

C. C. Chien*[1], R. A. Harrington[2], I. T. Li[3], C. H. Tsai[4], P. C. Tsai[5], C. L. Chang[6], W. T. Kao[7], C. C. Wu[8], C. L. Chu[9], H. Y. Hsu[3], F. W. Lung[10] and L. C. Lee[5], (1)*Kaohsiung Armed Forces General Hospital*, (2)*Johns Hopkins University*, (3)*Kaohsiung Medical University Chung-Ho Memorial Hospital*, (4)*Kaohsiung Municipal Kai-Syuan Psychiatric Hospital*, (5)*Johns Hopkins Bloomberg School of Public Health*, (6)*Graduate Institue of Medicine, Kaohsiung Medical University*, (7)*National Defense Medical Center*, (8)*Department of Psychology, Kaohsiung Medical University*, (9)*National Chung Cheng University*, (10)*Taipei City Hospital*

Background: The Social Communication Questionnaire (SCQ) is a screening instrument for Autism Spectrum Disorder (ASD). The screener is designed to match the Autism Diagnostic Interview-Revised (ADI-R). Studies conducted in Western countries that were designed as clinic-based or for high-risk populations (e.g., children in special education) reported strong indices of validity against the ADI-R. Because the ADI-R is subjective to a respondent's cultural bias, especially respondents who are from cultures different from that of Western populations, it may not be the best choice for diagnostic instrument in international studies. In light of the need for information from both caregiver's report and direct observation of the child in order to make an accurate diagnosis, a combination of the SCQ and ADOS can be considered for studies implemented in international settings.

Objectives: The purpose of this study is to examine the predictive ability of individual items

on the SCQ, and different cut-offs of the SCQ, on ADI-R, ADOS, and clinician-determined ASD diagnoses.

Methods: Study participants were drawn from a community-based autism study in Taiwan, where school children aged 6-8 were screened using the SCQ, followed by diagnostic evaluation using the ADOS, ADI-R, and a comprehensive evaluation by a child psychiatrist based on DSM-IV criteria if the SCQ is >=7. The study sample comprised 27 boys and 19 girls, and their primary caregivers, who completed the SCQ, ADOS, ADI-R, and who were evaluated by a child psychiatrist. Three study groups were classified based on the ADOS: ASD (n=12), subclinical (n=8), and unaffected (n=25). Similarly, 3 groups were defined based on the ADI-R: autism (n=4), subclinical (n=6), and unaffected (n=25). The 3 groups based on a child psychiatrist's clinical judgment were: ASD (n=7), other DD (n=24), and unaffected with ASD or other DD (n=15). Three cut-offs for the SCQ were used to define higher versus lower risk for ASD: 11, 15, and 22.

Results: Overall, the preliminary findings showed individual items of the SCQ, and the three SCQ cut-offs (11, 15, and 22) predict ADI-R diagnoses better than predicting ADOS diagnoses and clinical diagnosis made by a child psychiatrist.

Conclusions: It is not surprising that the SCQ better predicts the ADI-R classification than the ADOS or child psychiatrist's clinical judgment, as SCQ items were chosen from the ADI-R. Although some items significantly predict diagnostic classification, the majority of items and different cut-offs are not good predictors and do not discriminate diagnoses within each of the diagnostic evaluations (i.e., ADOS, ADI-R, and DSM-IV-based clinical judgment). This finding implies that the SCQ, when used alone, may not be a great screener for community-based or population-based autism studies. However, these results need to be interpreted with caution as the sample sizes for many subgroups are too small to provide sufficient statistical power to detect a statistically significant difference.

**121.132 132** Prenatal Antidepressant Exposure Is Associated with Risk for Autism and Attention Deficit-Hyperactivity Disorder in an Analysis of Electronic Health Records. C. C. Clements*[1], V. M. Castro[2], S. R. Blumenthal[1], H. R. Rosenfield[1], S. N. Murphy[1], M. Fava[1], J. L. Erb[3], S. E. Churchill[2], A. J. Kaimal[1], A. E. Doyle[1], E. Robinson[1], J. W. Smoller[1], I. S. Kohane[4] and R. H. Perlis[1], (1)*Massachusetts General Hospital*, (2)*Partners HealthCare System*, (3)*Brigham and Women's Hospital*, (4)*Brigham and Women's Hospital*

Background:

The etiology of Autism Spectrum Disorders (ASD) is complex, with both environmental and genetic factors contributing to risk. Building on rodent data suggesting behavioral abnormalities in offspring with prenatal exposure to serotonergic interventions, two observational studies have suggested association between ASD and prenatal antidepressant exposure. However, questions remain about the ASD risk of maternal psychiatric morbidity, rather than antidepressant treatment per se. Given that discontinuation of antidepressant treatment during or prior to pregnancy may also be associated with substantial health risks to both the mother and child, understanding the risks of treatments is of particular significance. We hypothesized that integrating electronic health records and birth certificates would allow detailed assessment of early environmental risks for ASD.

Objectives:

To assess 1) the association between prenatal antidepressant exposure and ASD, 2) the influence of maternal depression, and 3) whether the risk extends to other neurodevelopmental disorders, specifically ADHD.

Methods:

In the electronic health record of a large healthcare system, children who were delivered in the health system and later received a diagnosis of ASD (ICD-9 codes 299.0 Autistic Disorder, 299.8 Asperger's Syndrome, or 299.9 PDD-NOS) were selected for inclusion. A matched healthy control cohort and a comparison cohort with a diagnosis of ADHD (ICD-9 code 314.0) were also included. Parental demographic and maternal health data were linked to child data using birth certificates and electronic health records. Data on maternal psychiatric treatment and comorbidity were included. The association between prenatal antidepressant exposure and risk for ASD or ADHD was analyzed using logistic regression.

Results:

Maternal and child data records were successfully linked for 775 children with ASD, 2,724 matched controls and 1,578 comparison children with ADHD. Concordance between ICD-9 codes and diagnosis of ASD based on neuropsychological testing including ADOS administration was confirmed by manual chart review by an experienced pediatric neuropsychologist (PPV=0.73 for ASD group). Antidepressant exposure during pregnancy was associated with elevated risk for ASD (OR 1.92 [95% CI 1.31-2.78]) and for ADHD (OR 1.99 [95% CI 1.35-2.91]) in models adjusted for sociodemographic characteristics. When maternal psychiatric treatment and comorbidity and features of delivery were included in the models, the association with ASD remained significant.

Conclusions:

Consistent with other studies, our results show that prenatal antidepressant exposure is associated with ASD risk, but suggest that this risk may not be specific to ASD. The association does not appear to be confounded by maternal treatment for depression or other psychiatric disorders and comorbidities, nor by other pre- and peri-natal variables. However, the absolute risks are modest and should be weighed against the risks of discontinuing antidepressants. Findings also support electronic health record methodology as an efficient means of assessing pre- and peri-natal risks for ASD.

**121.133 133** Reliability of Maternal Self-Report of Medical Conditions and Obstetric Interventions. P. Krakowiak, D. J. Tancredi, I. Hertz-Picciotto and C. K. Walker*, *UC Davis*

Background: Pregnancy and perinatal complications have been implicated as risk factors in the etiology of autism spectrum disorders (ASD). Since acquisition and abstraction of data from medical records is both expensive and labor-intensive, most retrospective studies rely on maternal self-report of such events.

Objectives: We compared the reliability of maternal report of peri-gestational medical conditions at time points near to when conditions would have occurred and again two to five years later.

Methods: Ninety-four participants in the high-risk autism spectrum disorders cohort MARBLES (Markers of Autism Risk – Learning Early Signs) underwent structured telephone interviews during and immediately following pregnancy and again between two and five years later. Kappa statistics measured agreement between self-report during the peri-gestational period and recall two to five years later.

Results: While agreement between self-report of pre-pregnancy conditions; including diabetes, hypothyroidism and polycystic ovarian syndrome; over time was superb with kappas ranging from 0.85 to 1.00, recall of chronic hypertension was poor to fair (kappa 0.18, 95% CI -0.04, 0.40). Agreement of maternal recollection of vaginal bleeding and thyroid dysfunction during pregnancy over time was mediocre, each with a kappa of 0.58; more women reported having had vaginal bleeding or a thyroid disorder when asked during and just after pregnancy compared with recall years later. Women were also far more likely to report having had preeclampsia when interviewed within a few months of the diagnosis (kappa 0.26, 95% CI -0.18, 0.70). There was substantial agreement between reports over time of gestational diabetes and preterm labor, each with a kappa 0.82, though women interviewed years later tended to believe that their gestational diabetes was diagnosed earlier than women reporting within months of the diagnosis. Finally, agreement of maternal recall of amnioscentesis was better than that of chorionic villus sampling (kappa 0.61, 95% CI 0.39, 0.82 vs 0.26 95% CI -0.18, 0.70), perhaps reflecting confusion about the difference between the two procedures.

Conclusions: Studies attempting to link gestational conditions and obstetric interventions to the subsequent health and development of the offspring require careful attention to exposure assessment. Agreement of repeated measures of maternal recall regarding medical diagnoses and procedures included in this study varied by the condition under study, and women were more likely to remember less common events when asked close to the time the diagnosis or procedure would have occurred. This potential for exposure misclassification must be taken into consideration when designing and evaluating studies using self-report of pregnancy events.

**121.134 134** The Effect of Prenatal Air Pollution Exposure on Function and Severity in Children with Autism Spectrum Disorder. T. Kerin*[1], R. McConnell[1], I. Hertz-Picciotto[2], F. Lurmann[3], S. Eckel[1] and H. E. Volk[4], (1)*University of Southern*

*California*, (2)*University of California, Davis*, (3)*Sonoma Technology, Inc.*, (4)*USC - CHLA*

Background: Autism spectrum disorder (ASD) often has a heterogeneous presentation and broad range of impairment. Environmental factors, specifically prenatal air pollution, have been associated with ASD as well as poorer neurodevelopmental outcomes and increased cognitive deficits in separate studies.

Objectives: We examined the relationship between prenatal air pollution exposure and ASD severity, cognitive ability, and adaptive functioning among children with ASD.

Methods: Autism and ASD cases (N=331) from the Childhood Autism Risks from Genetics and the Environment (CHARGE) study were used for this analysis. CHARGE is a population based case-control study of California born children with autism, developmental delay or typical development who were between 24 and 60 months old at the time of assessment. Residential histories were geo-coded and used to develop estimates of average air pollution exposures during pregnancy. Regional air quality measures ($NO_2$, $PM_{2.5}$, $PM_{10}$, $O_3$) were assigned based on the EPA's Air Quality Monitoring Network and near roadway air pollution estimates developed using the CALINE4 line-source air-quality dispersion model. We examined Mullen Scales of Early Learning (MSEL) composite and subscale scores, Vineland Adaptive Behavior Scales (VABS) composite and subscale scores, and the Autism Diagnostic Observation Schedule (ADOS)–derived Autism Severity Score as continuous phenotypes.

Results: Higher regional $NO_2$ (and, to a lesser extent, $PM_{2.5}$) exposures during pregnancy were associated with lower values of many of the phenotypes considered. A 2 standard deviation (SD) increase in $NO_2$ (6.5 ppb) was associated with decreases of 11% (95% CI: -20%, -2%) on the VABS composite score, 26% (95% CI: -34%, -8%) on the composite MSEL score, 14% (95% CI: -24%, -4%) on the VABS communication subscale, 40% (95% CI: -49%, -16%) on the MSEL expressive language subscale, and 31% (95% CI:-45%, -8%) on the MSEL receptive language subscale. A 2 SD increase in $PM_{2.5}$ (6.7 $\mu g/m^3$) was associated with decreases in the MSEL expressive and receptive language of 27% (95%CI: -52%, 1.6%) and 29% (95%CI: -59%, 1.6%), respectively. Ozone, $PM_{10}$, and near roadway air pollution exposure were not associated with VABS or MSEL scores. We did not find an association between air pollution exposure during pregnancy and the Autism Severity Score.

Conclusions: These results suggest that $NO_2$ exposure during pregnancy may result in increased impairment, and specifically in more severe language and communication deficits, among children with ASD.

**121.135 135** The High Prevalence of Autism Spectrum Disorders Among Children with Intellectual Disabilities. C. C. Bradley*, L. A. Carpenter, S. Sergi, W. Jenner, J. Charles and L. B. King, *Medical University of South Carolina*

Background: Recent studies have estimated the prevalence of Intellectual Disability (ID) at 7 in 1,000 children (Boyle et al., 2011); however prevalence estimates relating to the rate of co-occurring autism spectrum disorders (ASD) have varied markedly based on the definition, assessment instruments, and study populations. Despite these discrepancies, several consistent trends have emerged. First, the prevalence of ASD appears to be inversely related to the severity of ID, such that ASD rates increase at lower levels of cognitive ability. Second, as cognitive functioning decreases, the gender gap between males and females in ASD prevalence also narrows. Last, it appears that many children with ID may have undiagnosed or unidentified comorbid diagnoses (Saemudsen et al., 2010), which showcases the importance of obtaining accurate prevalence rates for ASD in youth with ID in order to inform clinical diagnosis and ensure appropriate service utilization.

Objectives: (1) To estimate the prevalence of ASD in a population-based epidemiological sample of youth with ID; diagnosed through record review methodology. (2) To compare characteristics of youth with comorbid ID/ASD to youth with ID only.

Methods: Data for the present study came from SC-ADDM, which is one of several sites collaborating with the CDC to conduct ID surveillance in the United States. For each of the study years, all 8-year-old children with ID in the study area (the Coastal and Pee Dee regions of SC) were identified through screening and records abstraction at multiple educational and clinical sites. The de-identified records were linked with ASD surveillance data also collected by SC-ADDM

to determine the prevalence of ASD in youth with ID.

Results: Among youth born in 1994, 1996, 1998, and 2000, 1,818 met criteria for ID as defined by IQ < 70 on standardized instruments. Of these 1,818 youth, 38% (n = 698) also met ADDM case definition for ASD. Children with comorbid ASD/ID were more likely to be male (75% vs. 64%, $\chi^2$ (1) = 20.7, p < 0.05) and were more likely to have moderate to severe intellectual disability (43% vs. 16%, $\chi^2$ (1) = 67.5, p < 0.05) compared to those with ID only. Youth with ID/ASD were also significantly more likely to have low birth weight ($\chi^2$(1) = 5.7, p < 0.05).

Conclusions: This is the first study in almost twenty years to evaluate ASD prevalence and characteristics in a sample of youth with ID. Results suggest that almost 40% of children with ID have comorbid ASD, suggesting very high risk for ASD in this population. Increased ASD screening efforts may be needed in this group to ensure appropriate identification and intervention. Strengths include a large epidemiological sample utilizing independent review and assessment of ASD and ID, regardless of previous community diagnosis, which allows for more accurate prevalence estimates even for youth without formal clinical diagnoses. Obtaining accurate prevalence estimates of ASD in youth with ID is needed to inform clinical practice and ensure appropriate service utilization.

**121.136 136** The Validity of Social (Pragmatic) Communication Disorder. W. Mandy*[1], R. A. Wang[2], R. H. Warrington[3] and D. H. Skuse[3], (1)*University College London*, (2)*UCL, Institute of Child Health*, (3)*UCL Institute of Child Health*

Background:

The recent revision of the Diagnostic and Statistical Manual (DSM-5) created a new neurodevelopmental diagnosis of Social (Pragmatic) Communication Disorder (SPCD), characterised by severe difficulties with the social use of verbal and non-verbal communication, in the absence of autism spectrum disorder (ASD). The empirical literature on SPCD is exceptionally sparse, and so it is unclear whether SPCD is a distinct, coherent clinical entity. Specifically the following questions pertaining to the validity of SPCD have been raised: (1) are the symptoms of SPCD merely an epiphenomenon of other developmental problems, such as specific language impairment, attention deficit hyperactivity disorder (ADHD), internalising difficulties or conduct problems? (Norbury, 2013); (2) is SPCD really just a new name for elevated autistic traits which would previously have been labelled as pervasive developmental disorder - not otherwise specified (PDD-NOS) (Happe, 2011).

Objectives:

To identify and describe individuals meeting DSM-5 criteria for SPCD, in order to provide information on its validity.

Methods:

We used items from the Children's Communication Checklist (Bishop, 1998) and the Dimensional, Diagnostic and Developmental Interview (3Di), to create an algorithm which closely mapped onto DSM-5 criteria for SPCD. The algorithm was applied retrospectively within a sample of 1317 young people (mean age = 9.8 years, SD=3.4) who had been assessed at a clinic for high-functioning ASD. Young people with SPCD were compared to those with ASD and to clinic attenders without ASD on measures of language competence, autistic symptomatology and comorbid psychopathology.

Results:

Of the overall sample, 887 (67.4%) met criteria for DSM-5 ASD, and a further 97 (7.4%) met criteria for SPCD. The remaining 333 (25.3%) did not fulfil criteria for ASD or SPCD, and are designated 'clinical controls' in subsequent analyses. On both elements of the autism dyad, youths with SPCD scored intermediate between ASD and the clinical controls. Of the people with SPCD, a quarter (n=27, 27.8%) met DSM-IV criteria for PDD-NOS, with most others (n=59, 60.8%) not fulfilling DSM-IV criteria for any autistic diagnosis. Despite their greater difficulties with the social use of language, the SPCD participants did not score any worse than clinical controls on Children's Communication Checklist scales measuring 'syntax' and 'intelligibility and fluency', which are non-pragmatic aspects of language. Also, on the Strengths and Difficulties Questionnaire (Goodman, 1997), they did not show higher levels of social, conduct or internalising problems than controls, although they did have moderately higher levels of ADHD

symptomatology (Cohen's d=.43, p<.05). SPCD children had fewer peer problems (d=.52, p<.05) and were more prosocial (d=.52, p<.01) than those with ASD.

Conclusions:

On balance, our findings are supportive of the validity of SPCD. They do not support the claim that SPCD is a marker for specific language impairment, or that it is just an epiphenomenon of behavioural and emotional problems: compared to clinical controls, youths with SPCD had circumscribed social communication difficulties, without elevated levels of structural language problems or internalising and externalising psychopathology. Furthermore our findings do not support the notion that SPCD is merely the DSM-5 synonym for DSM-IV's PDD-NOS.

**121.137 137** Trends in ASD Co-Occurring Diagnoses in the Autism and Developmental Disabilities Monitoring Network. E. Rubenstein*[1], C. E. Rice[2], K. Van Naarden Braun[2], L. A. Schieve[2], M. S. Durkin[3], D. Christensen[4], A. V. Bakian[5], L. D. Wiggins[2], J. Daniels[6], L. B. King[7] and L. C. Lee[1], (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*Centers for Disease Control and Prevention*, (3)*University of Wisconsin-Madison*, (4)*CDC*, (5)*University of Utah*, (6)*UNC Gillings School of Public Health*, (7)*Medical University of South Carolina*

Background:

A recent report from the Autism and Developmental Disabilities Monitoring (ADDM) Network reported that 83% of 8-year-olds with an autism spectrum disorder (ASD) had at least one co-occurring developmental, neurologic, or psychiatric diagnosis (CD). Estimated prevalence of ASDs has significantly increased from 2002 to 2008. Little is known regarding the frequency of CDs among children with ASDs over time and whether specific CDs are increasing in relation to the increase in estimated prevalence of ASDs.

Objectives:

To examine the prevalence of CDs among children with an ASD and whether prevalence of CDs has changed.

Methods:

The ADDM Network is a biennial multiple source population-based surveillance system for ASDs and other developmental disabilities in 8-year-old children. Case identification is based on reviews of special education and health records. This study examined data from the 2002, 2006, and 2008 surveillance years. The sample was limited to ADDM sites for which >85% of children with ASDs had information on cognitive ability recorded. Altogether the sample included 4,051 children with ASDs identified at four sites. For each surveillance year, mean number of CDs was calculated and 95% confidence intervals (CI) were estimated using the Poisson distribution. To evaluate trends, extended Mantel-Haenszel tests were conducted, adjusting for site and whether the child's ASDs classification was based on review of education records only, health records only, or both. Tests were run for two variable types: 1) a categorical grouping of diagnosis type (developmental diagnoses, psychiatric diagnoses, neurological diagnoses, and possible causative medical diagnoses [such as birth defects or genetic disorders]); and 2) individual diagnoses subsumed within these 4 types.

Results:

In this sample of children with ASDs, the mean number of CDs increased significantly from 2.09 in 2002 (CI 1.99-2.19) to 2.32 in in 2008 (CI: 2.25-2.39) (p<0.001). In 2008 65.4% of children had one or more developmental CDs, 5.7% had one or more psychiatric CDs, 4% had one or more neurologic CDs, and 0.36% had one or more possible causative CDs. Thirty-six distinct CDs were identified: 13 developmental diagnoses, 13 psychiatric diagnoses, 6 neurological diagnoses, and 4 possible causative medical diagnoses. Of the 36 specific diagnoses, "developmental delay", a general diagnosis subsumed within the broader developmental diagnoses category was most frequent. Further, it increased from 56% in 2002 to 65% in 2008 (p<0.001). There were also significant trends in two other developmental diagnoses; language disorder increased and intellectual disability decreased. None of the conditions included in the psychiatric, neurologic, or possibly causal medical diagnoses categories changed from 2002-2008.

Conclusions:

CDs were prevalent in our population-based sample, which could complicate the identification and diagnosis of children with ASDs. Co-occurring developmental diagnoses were especially

prominent and one of these, developmental delay, has increased significantly since 2002. These results highlight the need for clinicians to be aware of the high prevalence of CDs in children with ASDs. CDs likely impact the observed phenotypic heterogeneity of ASDs and need to be considered in developing treatment strategies for children with ASDs.

**121.138 138** Trends in Autism Spectrum Disorders Incidence Among Children Born in Israel during 1992-2009: A Total Population Study. R. Raz*[1], M. Weisskopf[1], O. Pinto[2] and H. Levine[3], (1)*Harvard School of Public Health*, (2)*National Insurance Institute of Israel*, (3)*Hebrew University-Hadassah*

Background: The reported prevalence and incidence of autism spectrum disorders (ASD) are increasing worldwide. Diagnosis shifts, earlier age at diagnosis and clinical criteria, as well as environmental factors were suggested as explanations for this increase. Ascertainment of ASD is most probably influenced to a great extent by socio-demographic and cultural factors. These conditions limit the ability to conclude whether a real increase in incidence exists.

Objectives: Describe the incidence of ASD and its time trends in the total population of Israeli children born 1992-2009 by population group, and the prevalence of ASD in Israel by age 8 years.

Methods: We analyzed data from the records of the Israeli National Insurance Institute, a governmental welfare organization which tracks all Israeli residents. Case status was based on confirmation of unique child disability benefit due to ASD. The study population for incidence purposes consisted of all children born in Israel 1992-2009.

Results: Overall, 9,109 ASD cases among 2,431,649 children were included in the study. By 2011, ASD prevalence at age 8 was 0.49% (one in 203 children), but differed substantially by population group, with Israeli Arabs having 0.10%, Ultra-orthodox Jews with 0.30% and the general population with 0.76% (1.27% in boys, 0.23% in girls). There was a steep and consistent increase in ASD incidence with advancing birth cohorts born 1992-2004, stabilizing among those born 2005-2009. ASD cumulative incidence by age 8 years increased 10-fold during 1992-2003, from 0.049% to 0.49%. The trend for Israeli Arabs was different, with a later rise in incidence, only for birth cohorts born 2001-2009.

Conclusions: ASD incidence in Israel is rising, in accordance with worldwide trends. The segregation of rising incidence time trends by ethnic groups in Israel is compatible with a gradual process of increased awareness of medical staff, educational staff and the general public.

## 122 Molecular and Cell Biology

**122.140 140** 5-Hydroxymethylcytosine Is Increased in Autism Cerebellum and within the EN-2 Gene: Epigenetic Implications. S. J. James*[1], S. Shpyleva[2], S. Melnyk[1], O. Pavliv[1], T. Evans[1] and I. Pogribny[2], (1)*University of Arkansas for Medical Sciences*, (2)*National Center for Toxicological Research*

Background: 5-hydroxymethylcytosine (5-hmC) is created by the oxidation of 5-methylcytosine (5-mC) by TET enzymes and is most abundant in the brain, with highest concentration in Purkinje neurons. 5-hmC is now known to mediate the process of DNA demethylation and is often associated with activated neuronal genes. It's role as a stable epigenetic mark involved in the regulation of gene expression and it's association with MeCP2 binding and oxidative stress is less well defined. We recently reported DNA *hyper*methylation in the autism cerebellum and in the promoter region of the *EN-2* gene, a HOX transcription factor required for normal cerebellar development. Unexpectedly, promoter *hyper*methylation was associated with an *increase* in EN-2 protein and gene expression. Of note, the 5-mC binding protein MeCP2 does not bind strongly to intragenic 5-hmC. Reduced binding of the MeCP2 repressive complex could lead to local chromatin conformation changes and gene overexpression. It is important to note that current methods for detection of DNA methylation are not able to distinguish between 5-mC and 5-hmC; therefore, the independent contribution of each requires clarification for accurate interpretation.

Objectives: To simultaneously measure 5-mC and 5-hmC content in cerebellar tissue and within the *EN-2* gene and explore the association of 5-hmC with MeCP2 binding and with 8-oxo-dG, a marker of oxidative stress and DNA damage.

Methods: In 15 case and 15 control post mortem cerebellar samples, 5-mC, 5-hmC and 8-oxo-dG were quantified by LC/MS/MS after enzymatic digestion to DNA bases and expressed per µg DNA. The EpiMark™ 5-hmC and 5-mC Analysis Kit was used to quantify 5-hmC and 5-mC within

the *EN-2* gene. MeCP2 binding to DNA was determined using standard chromatin immunoprecipitation methods. TET enzyme gene expression was measured using quantitative reverse transcription real-time PCR.

Results: 5-hmC and 8-oxo-dG were significantly increased relative to control cerebellar samples and demonstrated a positive correlation whereas tissue glutathione levels were significantly decreased. Unexpectedly, 5-mC levels were also significantly increased in case compared to control cerebellum and were positively correlated with 5-hmC levels. These data suggest that elevated levels of 5-hmC were stable and independent of TET 5-mC demethylation activity. Consistent with this possibility, TET2 gene expression was not significantly different between case and control cerebellum samples. Within the EN-2 promoter region, 5-hmC and 5-mC levels were also significantly increased and positively correlated. MeCP2 binding to the EN-2 promoter was significantly decreased relative to control samples.

Conclusions: Previous reports of altered DNA methylation in autism brain need to be redefined in terms of the proportion of cytosine methylation due to 5-hmC and to 5-mC. The presence of 5-hmC in cerebellum appears to be a stable epigenetic mark that is independent of TET enzyme 5-mC demethylation. Increased levels of 5-hmC may decrease gene-specific binding of MeCP2 and lead to gene overexpression. Finally, the positive correlation between 5-hmC and 8-oxo-dG suggests the possibility that oxidative stress may be a non-enzymatic mechanism to oxidize 5-mC to 5-hmC.

**122.142 142** Cortical Interneuronal Subtypes in Autism. V. Martinez Cerdeno*, E. Hashemi and J. Ariza Torres, *University of California, Davis*

Background:

Patients with autism exhibit altered cognitive function that is revealed in EEG recordings as an imbalance of excitation to inhibition in the cerebral cortex. The concept that increased excitation / inhibition underlies the autistic cognitive phenotype is supported by the high prevalence of epilepsy in patients with autism. In addition, mouse models with misexpression of *Fmr1*, *MeCP2* or *Neuroligin 3* genes exhibit cortical interneuron defects. Furthermore, mice lacking the Dlx1 gene have fewer cortical interneurons and have age-dependent seizures and deficits in fear conditioning that resemble those seen in autism. Imbalanced excitation / inhibition could result from multiple alterations of brain structure and/or function, including an alteration in the number or ratio of specific interneuron subtypes in the cerebral cortex. The majority of interneurons in the cerebral cortex can be classified in three major subtypes: parvalbumin+ (PV), calbindin+ (CB), or calretinin+ (CR) interneurons. These interneuron subtypes have distinct morphologies, physiological properties, and connectivity patterns.

Objectives:

We hypothesize that an alteration in the number of interneurons within each interneuronal subtype in the cerebral cortex could explain, at least in part, the altered cognition phenotype in autism.

Methods:

To test this hypothesis we collected cortical tissue from subjects with autism and typically developed control subjects, and analyzed cortical areas that are affected in autism: the prefrontal and temporal cortex. We optimized a method for triple immunostaining together with Nissl in human cortical tissue, quantified the number of interneurons that express CB, CR, or PV, and calculated ratios for the number of interneurons expressing each marker. Determining whether the ratio in the number of specific interneurons is altered in autism will address one of the mechanisms that could alter the excitation / inhibition balance in the cerebral cortex.

Results:

We are collecting data on this project. Our preliminary data suggests that the ratio of interneurons that express CB, CR, and PV changes across ages. We predict that there will be an alteration in the ratio of interneurons that express CB, CR or PV in the cerebral cortex of subjects with autism.

Conclusions:

Determining whether the ratio of interneuron subtypes is altered in the autistic brain will address one potential mechanism that could alter the excitation / inhibition balance in the cerebral

cortex. Altering the ratio or number of cortical interneuron subtypes would impact the functioning of cortical circuitry.

**122.143 143** Decreased mTOR Signaling Via p70S6K/eIF4B Is Associated with Loss of the Excitatory Postsynaptic Marker PSD-95 in Autism. C. Nicolini*[1], G. Baj[2] and M. Fahnestock[1], (1)*McMaster University*, (2)*University of Trieste, BRAIN Centre for Neuroscience*

Background:

Dendritic spines are small protrusions from dendrites where most excitatory synapses occur. Similar to other neural disorders including mental retardation, schizophrenia, fragile X and Rett syndromes, changes in spine number and shape lead to synaptic dysfunction and perturbed neuronal circuit development in autism. Local translation of dendritic mRNAs has been shown to play a pivotal role in spine morphogenesis and synaptic plasticity. Thus, we hypothesized that disruptions in dendritic mTOR-dependent translation initiation may contribute to spine pathology in the autistic brain. We previously found decreased components of the mTOR pathway in postmortem fusiform gyrus of subjects with autism compared to controls. mTOR influences protein translation at spines via two downstream effector pathways which are responsible for promoting translation of different pools of mRNAs. One cascade involves p70S6K and eukaryotic initiation factor 4B (eIF4B) and regulates translation of proteins belonging to the translation machinery such as elongation and initiation factors and ribosomal proteins, while the other comprises eukaryotic initiation factor 4E-binding protein 1 (4E-BP1) and eukaryotic initiation factor 4E (eIF4E) and controls translation of 5′ capped mRNAs coding for structural and functional synaptic proteins.

Objectives:

We aimed to examine which mTOR-mediated downstream signaling pathway is disrupted in autism and whether this disruption is associated with changes in PSD-95, a marker of excitatory synapses.

Methods:

Phospho-mTOR, mTOR, p70S6K, eIF4B, 4E-BP1, eIF4E and PSD-95 were measured by Western blotting in postmortem fusiform gyrus of 11 autism and 13 control subjects.

Results:

Significantly decreased phospho-mTOR, mTOR, p70S6K and eIF4B protein levels were observed in the fusiform gyrus of autism compared to control subjects. Surprisingly, no significant changes in 4E-BP1 and eIF4E protein expression were found in autism versus control fusiform gyrus, supporting the specificity of the p70S6K/eIF4B pathway deficit. Lastly, a significant reduction in PSD-95 protein was determined in autism subjects compared to controls.

Conclusions:

Decreased mTOR expression and activation were found in fusiform gyrus of autistic subjects compared to controls. Disruptions in mTOR downstream signaling pathways were specific to the p70S6K/eIF4B pathway, suggesting reduced translation of mRNAs mainly encoding components of the translational machinery. Remarkably, dysfunctional mTOR signaling was associated with a significant decrease in protein expression for the excitatory synaptic marker PSD-95, suggesting a reduction in excitatory synapses. In conclusion, reduced signaling via mTOR/p70S6K/eIF4B may result in decreased spine protein synthesis and thereby lead to loss of excitatory synapses. Reduced excitatory synapses in turn might perturb development and maintenance of functional cortical circuits and thus contribute to autism's cognitive and behavioural deficits.

**122.144 144** Enteric Nervous System Dysfunction in Autism Spectrum Disorder: Development of an in Vitro Ips-Derived Model System Using Patient Cells. A. L. Wagoner*[1], D. L. Mack[2] and S. J. Walker[1], (1)*Wake Forest University Health Sciences*, (2)*Institute for Stem Cell & Regenerative Medicine*

Background: Autism Spectrum Disorders (ASDs) are characterized by central nervous system (CNS) dysfunction that manifests in behavioral and cognitive deficits. A number of genes, especially those that code for synaptic proteins, have been shown to harbor mutations and/or deletions that result in functional consequences in the CNS of ASD individuals. Many of these genes, for example Shank3 and Neuroligin3, are also expressed in the enteric nervous system (ENS), making it likely that mutations causing CNS

dysfunction are also operating at the level of the ENS. In order to explore this relationship we have undertaken the development of a patient-specific induced pluripotent stem cell (iPSC)-derived *in vitro* model system that can be used to generate and functionally characterize enteric neurons.

Objectives: The overall goal of this project is to develop a model system to study ENS dysregulation in ASD children. We propose to do this by selecting patients from the Autism Genetics Resource Exchange (AGRE) who meet the criteria for suspected CNS and ENS involvement and who have a functionally-relevant single nucleotide polymorphism (SNP) and/or deletion in a key synaptic protein-coding gene. Cells from these individuals (and controls) will be used to differentiate enteric neurons which can then be assessed for function using established *in vitro* assays.

Methods: The steps involved in our model development are fourfold: (1) identify ASD individuals who have ENS involvement (as measured by gastrointestinal dysfunction; e.g. GERD or hypomotility) *and* CNS involvement, and who have a known mutation/deletion in at least one of the genes known to negatively impact the function of a key synaptic protein, (2) use lymphoblastoid cell lines (LCLs) from these individuals to generate induced pluripotent stem cells, (3) direct the patient-specific iPSCs down neuronal lineages to make enteric neurons, and (4) characterize the function of these neurons, compared to those derived from individuals with unaffected synaptic proteins, in a smooth muscle co-culture system.

Results: Epstein Barr Virus immortalized-LCLs were obtained from two male sibling probands from the AGRE: one with a SNP in the gene coding for Shank3 and another SNP in the gene coding for Homer1; the second with only the Homer1 SNP. IPSCs, generated from EBV-LCLs transfected with Epi5 Episomal iPSC reprogramming plasmids, were apparent at Day16 post-transfection. Clonal iSPC lines are being evaluated for patient-specificity, normal karyotype, expression of pluripotency markers, and loss of OriP/EBNA-1 expression vectors. In parallel experiments, neural progenitor cells and neural crest cells, differentiated from human embryonic stem cells, showed proper gene expression and cell morphology. Neural lineage differentiation methods have now been optimized and will be applied to the ASD-specific LCL-derived iPSCs for the generation of enteric neurons.

Conclusions: Using a state-of-the-art reprogramming system, LCLs from ASD individuals in the AGRE repository have been used to generate iPSCs. We have also demonstrated that stem cells can be differentiated to neural progenitor and neural crest cells. Our next step will be to differentiate the ASD-specific iPSCs into enteric neurons and then compare their function to enteric neurons derived from non-ASD cells.

**122.145 145** Functional Analysis of PTCHD1 Reveals Interactions with Synaptic Machinery and Involvement in the Hedgehog Pathway. K. Mittal*[1], K. Sritharan[1], B. Degagne[1] and J. B. Vincent[2], (1)*Centre for Addiction and Mental Health*, (2)*Centre for Addiction & Mental Health*

Background:

Autism Spectrum Disorder (ASD) includes a range of complex neurodevelopment disorders. Approximately 75% have lifelong disability requiring substantial social and educational support.

Objectives:

This study is focused on investigating the complex functional aspects of a recently identified gene -- PTCHD1, and how its disruption leads to Autism Spectrum Disorder and/or Intellectual Disability. The insight gained will help in more precise phenotypic characterization of the individuals with disrupted PTCHD1.

Methods:

Firstly, we sought to identify PTCHD1 splice variants that might have higher or more specific expression in brain, and may thus be more relevant to the neurobiology in individuals with autism and/or intellectual disability who have PTCHD1 mutations. We performed mRNA expression analysis using mRNA from multiple tissues, including brain regions. Western blots were performed to confirm these findings.

To establish the involvement of PTCHD1 in the Hedgehog (Hh) signaling pathway, expression analysis was carried out with Hh pathway genes. We also probed for sub-cellular localization of PTCHD1 in cilia. Immunoprecipitation studies and expression studies were also performed to identify

potential synaptic interacting partners or downstream targets.

Results:

We identified a new transcript skipping exon 2 which is predicted to encode a 542 amino acid protein in comparison to the 888 amino acid protein encoded by the PTCHD1 long isoform. It has just 4 transmembrane domains, and encodes a 62 kDa protein as compared to 12-transmembrane domains in the long isoform and a 101 kDa protein. We also found the presence of an additional exon upstream of exon 1. The quantitative expression analysis demonstrates that expression of these PTCHD1 transcripts is highest in human cerebellum.

The quantitative expression analysis with over expression of PTCHD1 revealed increased levels of neuroligin and neurexin mRNAs. Immunoprecipitation studies indicate interactions including between PTCHD1 and Postsynaptic Density protein 95 (PSD-95) proteins. We also confirmed localization of PTCHD1 in cilia- which is where Hh receptors PTCH1 and 2 function, as well as evidence of PTCHD1 dimerization.

Conclusions:

The new PTCHD1 transcripts seem to have an important role to play in the brain and in its sub regions, thus, these transcripts and encoded isoforms may be more relevant to autism and intellectual disability. The interacting partners would help us elucidate the etiology underlying the disease phenotype.

The quantitative expression analysis with over expression of PTCHD1 suggests a possible regulatory effect of PTCHD1 on genes that encode synaptic proteins. PSD-95 determines the size and strength of synapses in the postsynaptic density of neuronal excitatory synapses, and this putative interaction with the PTCHD1 protein could be important to elucidate disease etiology.

The Hh pathway plays an important role in embryonic development and adult stem cell functioning. Protein components of primary cilia are required for Hh signaling. We hypothesize that PTCHD1 localization to primary cilia could inhibit the Hh pathway in the developing brain, also that PTCHD1, as a chemosensor for extracellular SHh, may influence generation or functioning of synapses.

**122.146 146** Oxidative Stress Induces Mitochondrial Dysfunction in a Subset of Autism Lymphoblastoid Cell Lines. S. Rose*[1], R. E. Frye[2], J. C. Slattery[2], R. A. Wynne[3], M. Tippett[4], S. Melnyk[1] and S. J. James[1], (1)*University of Arkansas for Medical Sciences*, (2)*Arkansas Children's Hospital Research Institute*, (3)*Arkansas Children's Hospital*, (4)*ACHRI*

Background: Mitochondrial dysfunction (MD) is associated with autism spectrum disorders; yet little is known about the etiology of MD or how it might interact with other physiological abnormalities associated with autism, such as oxidative stress. Primary lymphocytes and lymphoblastoid cell lines (LCLs) derived from children with AD exhibit decreased glutathione-mediated redox capacity and higher reactive oxygen species (ROS) compared to controls. This decreased ability to counter endogenous ROS production in AD immune cells may result in increased vulnerability to oxidative damage and mitochondrial dysfunction during pro-oxidant exposures.

Objectives: We sought to determine whether mitochondrial respiration in AD and age and gender-matched control LCLs differed at baseline and in response to ROS. We hypothesized that upon increasing ROS, a subgroup of AD LCLs will demonstrate abnormal reserve capacity, a measure the mitochondrial ability to respond to physiological stress. To further investigate whether mechanisms to compensate for increased ROS differed between control and AD LCLs, we measured glycolysis as an intracellular compensatory mechanism and uncoupling protein 2 (UCP2) content as an intramitochondrial compensatory mechanism. UCP2, a major control mechanism for reducing ROS at the inner mitochondrial membrane, is up-regulated in many cell types under conditions of chronic mitochondrial oxidative stress.

Methods: Mitochondrial oxygen consumption and glycolysis were measured using Seahorse extracellular flux (XF) technology. We compared bioenergetic profiles from 25 AD and control LCL pairs, matched by age and gender, before and after 1 h exposure to 5-15μM DMNQ (2,3-dimethoxy-1,4-napthoquinone), a ROS generator. Intracellular glutathione was measured by HPLC, intracellular ROS by CellRox green fluorescence and flow cytometry, UCP2 content by western

blot, and mitochondrial DNA copy number by real-time PCR.

Results: Compared to controls, AD LCLs exhibited abnormally elevated reserve at baseline that was severely depleted with increasing ROS. The changes in reserve capacity in AD LCLs resulted from higher ATP-linked and maximal respiratory capacity at baseline and a marked increase in proton leak with increasing ROS. These abnormalities were driven by a subgroup of eight (32%) of 25 AD LCLs, and further investigation revealed that this subgroup produced increased ROS and demonstrated a greater reliance on glycolysis and on UCP2 in attempt to regulate oxidative stress at the inner mitochondria membrane. Mitochondrial copy number was not different between the two AD subgroups. Glutathione redox capacity was reduced in the AD LCLs compared to controls but was not different between the two AD subgroups.

Conclusions: This study suggests that a significant subgroup of AD children may have altered mitochondrial function rendering them more vulnerable to a pro-oxidant microenvironment derived from intrinsic and extrinsic sources of ROS such as immune activation and pro-oxidant environmental toxins. These findings are consistent with the notion that AD is caused by a combination of genetic and environmental factors. An underlying defect in mitochondrial function could be a key deficit in AD affecting high energy demanding organs, particularly the brain and immune system, and could account for the commonly reported systemic abnormalities associated with ASD, such as immune dysfunction.

## 123 Repetitive Behaviors and Interests

**123.147 147** Increased Intra-Participant Variability in Olfactory Sensitivity Correlates with Autistic Trait Levels. D. R. Simmons* and A. E. Robertson, *University of Glasgow*

Background: It is now well established that both a diagnosis of Autism Spectrum Disorder (ASD) and/or an increased level of autistic traits results in increased reporting of sensory difficulties (Robertson & Simmons, 2013). Typical olfactory symptoms reported by individuals with ASD include difficulties in tolerating "perfumed" environments like pharmacies and restaurants, problems being around people who have recently been smoking, or, alternatively, a preference for strong-tasting foods like garlic and chilli. Despite these data, laboratory-based findings on olfactory performance in ASD have provided mixed results, with a number of studies finding no significant differences between ASD and control populations (e.g. Tavassoli & Baron-Cohen, 2012).

Objectives: To obtain data on olfactory performance in a sample taken from the general population, whilst simultaneously measuring autistic trait level and reported sensory symptoms.

Methods: 106 adults participated in the experiment (mean age, 24 years; 74 females). Olfactory performance was measured using "Sniffin' sticks" (Burghart, Messtechnik), a standardized method for measuring olfactory detection, discrimination and identification. Autistic traits were measured using the Autistic Spectrum Quotient (AQ; Baron-Cohen et al, 2001). A subset of participants also filled in a questionnaire about their own sensory issues (Robertson & Simmons, 2013). For some analyses, we separated the top 17 highest scorers in the AQ (27.8 ± 5.6) from the 18 lowest scorers (6.3 ±1.6), representing approximately the top and bottom 15% of the sample.

Results: There was no significant relationship between AQ score and olfactory detection thresholds, neither did the high AQ scorers differ significantly from the low AQ scorers. However, we also obtained a measure of intra-participant variability: the variance in individual mean detection threshold. We found a small, but significant, correlation between this variability measure and AQ score (r=.266, $p<.01$, $R^2=.071$) and a significant difference between high- and low AQ scorers [$t(21.71) = 2.23$, $p<.05$, $r=.277$]. There were no significant correlations with AQ score, or significant differences between high and low scorers, in measurements of olfactory discrimination or identification thresholds, even after controlling for gender and native language. We did, however, find a significant correlation between AQ score and reported sensory difficulties [$r=.433$, $p<.001$, $R^2=.187$], confirming previous results.

Conclusions: These data suggest that whilst there are no differences in mean olfactory detection, discrimination or identification performance with varying autistic traits, detection threshold variability, within a given individual, is

higher in those scoring higher on the AQ. Therefore an apparent lack of difference in mean scores on sensory threshold tests could mask an underlying variability in performance. One potential cause of intra-participant variability in threshold performance is the existence of significant levels of internal neural noise, which can alter perception on a moment-to-moment basis (Dinstein et al, 2012; Milne, 2011; Simmons et al, 2009). Higher internal noise levels may thus explain the apparent conundrum of increased sensory difficulties with increasing autistic trait levels which are unaccompanied by a change in mean thresholds.

**123.148 148** The Relationship Between Repetitive and Stereotyped Behavior and Social-Communicative Skills in Young Children with ASD. A. Hellendoorn*[1], L. Wijnroks[1], E. Van Daalen[2] and P. Leseman[1], (1)*Utrecht University*, (2)*University Medical Centre*

Background: Repetitive and stereotypes behaviors (RSB) have received far less attention in autism research compared to deficits in the social-communicative domain (Richler, Huerta, Bishop & Lord, 2010; Lewis & Bodfish, 1998). Moreover, not much research has been done on the relationship between RSB and social communication skills (Ray-Subramanian & Weismer, 2012). Nevertheless, understanding of RSB is important, because of its interference with different aspects of functioning in children with ASD, especially with the possibilities to learn from and attend to the world around them (Richler et al., 2010). Therefore, research should focus on examining possible relationships between RSB and symptoms in social and communication domains (Richler et al., 2010; Watt, Wetherby, Barber & Morgan, 2008).

Objectives: The present study aimed (1) To examine the relationships between RSB and social communicative skills in children with ASD. It is hypothesized that a higher frequency and/or duration of RSB is negatively related to social-communication skills. (2) To examine the relationships between RSB and the severity of ASD symptoms in young children. It is predicted that a higher frequency and/or duration of RSB is positively correlated to severity of ASD symptoms in young children.

Methods: Fifty-five young children with ASD were included in this study. RSB was assessed by coding the frequency and duration of RSB on videotaped observations of the ADOS (33.05 ± 9.83 months). The level of social-communicative skills was measured using the subscale interpersonal relationships of the Vineland SEEC (46.34 ± 6.55) and the subscales language and communication and reciprocal social interaction of the ADI-R (30.29 ± 7.48 months). Severity of ASD was assessed using the total scores of the ADOS and the ADI-R and interpreting them as spectrum scores. A series of stepwise multiple regressions were conducted to evaluate whether RSB are related to social-communicative skills and severity of ASD.

Results: As hypothesized a negative relationship with a medium effect size was found between the duration of RSB and social-communicative skills. Secondly, as hypothesized a positive relationship with a medium effect size was found between the duration of RSB and severity of ASD.

Conclusions: The findings of this study indicate that a prolonged engagement in RSB is negatively related to social-communicative skills and positively related to severity of ASD. These findings are in line with other studies, which show that RSB can negatively influence the development of social and communication skills and overall development, because of its interference with learning opportunities (Bruckner & Yoder, 2007; Ray-Subramanian & Weismer, 2012; Watt et al. 2008). This study adds to the limited research between RSB and social-communication skills and may enhance the understanding of developmental trajectories of ASD, including cascades across domains.

**123.149 149** Descriptive Analysis of the B Codes: Understanding Restrictive and Repetitive Behaviors in a Clinical Population. K. S. D'Eramo*[1], M. J. Palmieri[2], M. D. Powers[1], T. M. Newman[2], C. M. Cotter[1] and K. Marshall[1], (1)*The Center for Children with Special Needs*, (2)*Center for Children with Special Needs*

Background: A primary change to diagnostic criteria in DSM-5 involves requirements for restrictive and repetitive behaviors (RRBs). While DSM-IV-TR permitted diagnosis for individuals who did not meet any RRB symptom criteria, DSM-5 criteria require that an individual meet at least two of four RRB symptoms. While proponents argue that the change improves specificity, some research suggests the change may impact diagnoses for individuals who previously qualified for ASD under DSM-IV-TR.

Objectives: A current challenge for clinicians completing diagnostic evaluations is to better understand RRB diagnostic codes and to properly classify behavioral symptoms. By investigating the specific symptoms coded under each of the four codes, we investigate patterns of RRBs across individuals who do and do not qualify for ASD diagnosis under DSM-5 criteria.

Methods: We evaluated 254 individuals presenting for psychological evaluation at an ASD specialty center. The comprehensive assessment included developmental history, cognitive testing, diagnostic (ADOS2) and adaptive assessment (Vineland-II caregiver interview). Licensed psychologists completed the evaluations. Following assessment, psychologist(s) completed a rating form indicating which specific DSM-IV-TR and DSM-5 diagnostic codes the individual met, including (for a subset n = 137) the specific RRB symptoms endorsed under each of the four DSM-5 RRB codes.

Results: Of these 254 individuals, 234 (92.1%) received a clinical diagnosis of ASD. All 234 (100%) met criteria on DSM-IV-TR while only 84.2% met DSM-5 criteria for ASD. Analysis of the 37 individuals who met criteria on DSM-IV-TR but not DSM-5 ("lost diagnosis") revealed that the most common symptom profile (54.1%) was one in which individuals met criteria for all three social-communication symptoms (A codes) but only one of RRB symptom (B codes). We subsequently attempted to characterize the symptom profiles of a subset of individuals (n=137) upon whom specific symptom data for the four B codes were available.

Among individuals who met DSM-5 criteria (n=107), the modal number of B codes endorsed was 4 (range 2 – 4, mean = 3.13) and the average number of RRB symptoms endorsed was 4.77 (range 2 – 12). Among individuals who "lost diagnosis" under DSM-5 (n=20), 11 (55%) lost specifically because they had only one B code but all three A codes. In this group, the vast majority (73%) met RRB criteria for excessively circumscribed or perseverative interests. In contrast, the same symptom was scored in only 26% of the individuals who met DSM-5 criteria. Individuals who met under DSM-5 were most likely to score for adverse response to specific sounds or textures, simple motor stereotypies, and insistence on same routine or food.

Conclusions: Consistent with prior research, results suggest that new requirements for RRBs may impact diagnosis of ASD under DSM-5 criteria. Results suggest differences in RRB symptom patterns which may help to identify those at greatest risk for failure to meet DSM-5 criteria and lend support to concerns about the impact on individuals who were more likely to be diagnosed with Asperger Syndrome or PDD:NOS under DSM-IV-TR .

**123.150 150** The Sensory Experiences of Children with Autism Spectrum Disorders and Complex Needs: A Qualitative Analysis. A. E. Robertson* and D. R. Simmons, *University of Glasgow*

Background: A recent review demonstrated that sensory issues are common in ASDs, albeit heterogeneous in their nature (Ben-Sasson et al., 2009). This review substantiated accounts that have been written by people with ASD (e.g. Grandin & Scariano, 1996; Williams, 1998), in which the authors describe overwhelming responses to certain stimuli. In order to gain insight about the nature of sensory experiences of children with ASD, we held a focus group for caregivers of children and young adults with autism and complex needs, as this is a particularly hard-to-reach population.

Objectives: To explore both positive and negative aspects of the sensory experiences of children and young adults with autism and other complex needs, from the point of view of their caregivers. We were also interested in exploring the impact that these sensory experiences can have on the family as well as the individuals themselves.

Methods: A focus group with nine caregivers of eight children and young people with autism and complex needs was conducted. The diagnoses of the children and young people were: autism only (n=2), autism and Down's Syndrome (n=3), autism and blindness (n=1), autism and cortical dysplasia (n=1), autism and Angelman's Syndrome (n=1). Participants were recruited via a gate-keeper who worked for a local charity that supports people with sensory impairment and their families. The focus group was on the topic of 'Sensory issues in Autism Spectrum Disorders' and took 1hr 33min to complete. Data were transcribed then analysed using a general inductive qualitative approach, which is a similar approach to thematic analysis (Thomas, 2006). The first author coded the transcript, with the

second author coding 20% in order to ascertain inter-rater reliability. A Kappa's Coefficient of .813 was obtained, demonstrating a high level of agreement.

Results: Two main findings emerged from these data. Firstly, the caregivers described that experiencing unpleasant sensory stimuli was extremely difficult. This theme was composed of three sub-themes: emotional consequences, physical consequences and social consequences. Caregivers reported these three sub-themes for both their child and themselves. Secondly, caregivers discussed how they attempted to ameliorate the impact of sensory experiences (or their repercussions) themselves. Strategies employed fell into two sub-themes: using positive sensory experiences and employing a variety of distraction or avoidance techniques.

Conclusions: Firstly, caregivers reported that their children experienced discomfort when faced with certain types of sensory stimuli, which were broadly categorised as physical (e.g. self-harm), emotional (e.g. fear and anxiety) and social (e.g. avoidance of certain environments) implications. Caregivers also experienced physical (e.g. being physically hurt), emotional (e.g. distress at their child's discomfort) and social (e.g. being unable to attend family gatherings) consequences of the negative sensory experiences of their child. Secondly, caregivers mentioned that positive sensory experiences were effective in reducing anxiety or the effect of negative sensory experiences (e.g. massage or watching light streaming through leaves). Caregivers reported trying to integrate their child into their community as much as possible. They also discussed their fears for their child and how aware they had to be of possible triggers for their child.

**123.151 151** Early Developmental Patterns of Repetitive Behavior in Autism Spectrum Disorders. K. E. Unruh*[1], J. W. Bodfish[2], L. Turner-Brown[3] and B. Boyd[3], (1)*Vanderbilt Brain Institue*, (2)*Vanderbilt University School of Medicine*, (3)*University of North Carolina at Chapel Hill*

Background: While social and communication impairments have been the focus of a growing amount of research in autism spectrum disorders (ASD), little is known about the phenomenology and development of restricted repetitive behaviors (RRBs) in young children with ASD. RRBs can cause significant impairment for individuals with ASD and their families; such rituals may consume large amounts of time and interfere with daily activities. These behaviors may be of particular significance due to research suggesting RRBs interfere with observational learning, play skills, and responses to auditory stimuli. Previous work has also suggested the more time a child spends engaging in RRBs, the less time he or she spends exploring his or her environment. Thus, RRBs may replace or prevent normal exploration and experience-dependent learning during critical periods of development. Lastly, little is known about the relationship between RRBs and problems with mood and behavior (e.g., anxiety and hyperactivity) in ASD. Parents and caregivers often report that interruption or prevention of certain RRBs can result in increased levels of anxiety or tantrums in some children with ASD, which suggests a possible relationship between these behaviors.

Objectives: To describe and compare the phenomenology and development of RRBs in young children with ASD to those that occur in typical development (TYP) and developmental delay (DD), and to identify types of mood and problem behaviors that may be associated.

Methods: The sample included children between the ages of 2 and 5 years, with either ASD (n=62, $M_{age}$=50.5 m), TYP (n=65, $M_{age}$=46.5 m), or DD (n=18, $M_{age}$=49.0 m). A set of standardized, psychometrically-sound parent rating scales were used to measure the domains of interest. The Repetitive Behavior Rating Scale-Revised (*RBS-R*) is a 43-item rating scale and was used to measure 5 types of repetitive behavior: Stereotyped Behavior, Self-Injurious Behavior, Compulsive Behavior, Ritualistic/Sameness Behavior, and Restricted Behavior. Mood and problem behaviors were assessed using the Nisonger Child Behavior Rating Form (*NCBRF*), a 70-item questionnaire developed to assess behavior and emotional problems in children, such as anxiety and conduct problems.

Results: Results suggest that a variety of RRBs are more prevalent in children with ASD (all *p*s < .001) beginning at age 2. Specifically, levels of both Ritualistic/Sameness behavior and Restricted Interests were found to be significantly higher in ASD ($p < .01$), but did not differ between TYP and DD. Cross-sectional analyses revealed that all types of RRBs increased from age 2 to 5 in the ASD group only (*p*s < .05). In ASD, anxiety was

strongly associated with the presence of "higher level" (e.g., Ritualistic/Sameness) RRBs ($p$ < .001).

Conclusions: Our findings suggest that a variety of repetitive behaviors emerge early in children with ASD, with Ritualistic/Sameness and Restricted Interests behaviors specifically increased in occurrence with respect to ASD. Additionally, the association between RRBs and mood/problem behaviors in ASD indicates these behaviors (particularly anxiety) could play a role in the expression of RRBs.

**123.152 152** Antecedents and Characteristics of Missing Incidents and Recoveries. M. Rowe*, L. O. Smith, H. J. Spring, J. R. Farias, M. Morley, K. Armstrong and S. Arnold, *University of South Florida*

Background: Children with autism spectrum disorders (CwASD) are at increased risk for missing incidents and the associated dangers. There is little guidance as to how to prevent or address these behaviors, and as such, caregivers report additional caregiving stress, sleep problems and/or isolation.

Objectives: The purpose of this study was to better understand the antecedents of missing incidents, the circumstances under which a missing incident occurred, the characteristics of how children are found and to determine any predictors of a missing child not surviving the incident.

Methods: The study was a retrospective review of media reports of missing CwASD. Seventy-five analyzable cases were retrieved using a systematic search strategy. Inclusion criteria included: specific indication the child was diagnosed with ASD, aged 3-17 years, reported in an official news media, and have adequate data to be able to understand the circumstances of the event.

Results: Missing incidents occurred across the age span with a higher ratio of males, from all living settings and throughout the U.S. Most children left on foot, but a few utilized wheeled or public transportation. In a third of the cases, there was notation of a previous missing incident. The most common care provider at the time of the incident was a parent who was generally in close proximity to the child. In 10% of the cases, the child was intentionally left alone, usually to and from the school/bus setting. The children went missing from both the home and community settings which included: playgrounds and recreation areas and visiting friends/relatives. Most children were observed just minutes before a missing incident by the care provider. Sometimes the children were left intentionally unsupervised while the parent was in a different area, i.e. playing in the yard while the parent was inside. Sometimes the care provider was distracted and there was an unintentional gap in supervision. The strongest predictor of not surviving a missing incident was age with younger children having 22 times greater risk of death.

Conclusions: Missing incidents in CwASD are ubiquitous in terms of location and circumstance as incidents occurred throughout the normal set of activities for a child. Few predictors could be identified – agitation and an extended stay in a different location seemed to associated with some incidents. Some children were able to leave a safe situation even during times that care providers were intending direct supervision; other times children left in circumstances they previously negotiated independently. Further research is critical to understanding mechanisms of prevention and rapid location, particularly of young children.

**123.153 153** Impact of Risperidone on Repetitive Behavior in Autism: Results from Research Units on Pediatric Psychopharmacology (RUPP) Autism Network Trials. D. G. Sukhodolsky*[1], E. I. Anderberg[2] and L. Scahill[3], (1)*Yale School of Medicine*, (2)*University of Washington*, (3)*Marcus Autism Center*

Background: The Children's Yale Brown Obsessive Compulsive Scales modified for youth with with ASD (CYBOCS-ASD) has demonstrated reliability and validity for measuring repetitive behavior in this population (Scahill et al., 2006). The CYBOCS-ASD was used as an outcome measure in two randomized clinical trials focused on repetitive behavior. The first study evaluated the efficacy of the selective serotonin reuptake inhibitor, citalopram (King et al., 2009). The second trial examined the efficacy of an oral-disintegrating formulation of fluoxetine (Autism Speaks, 2009). In each of these studies, there was no difference between drug and placebo on the CYBOCS-ASD.

Objectives: The purpose of the present report is to examine the sensitivity of the CYBOCS-ASD to detect change in repetitive behavior in a large

sample of well-characterized children with ASD treated with risperidone.

Methods: Data for this set of analyses was compiled from two federally-funded, multisite, randomized clinical trials (Aman et al., 2009; RUPP Autism Network, 2002) and included 225 subjects (187 boys and 38 girls, age 4 to 17 years). In the first trial, subjects were randomly assigned to risperidone (n=49) or placebo (n=52) for eight weeks under double-blind conditions. All 101 participants In Study 1 met DSM-IV criteria for autistic disorder (RUPP Autism Network, 2002). Study 2 included 124 children with autistic disorder, Asperger's disorder or Pervasive Developmental Disorder. In Study 2, we used an unbalanced randomization whereby 49 subjects were assigned to risperidone alone and 75 were assigned to risperidone plus parent training. An independent evaluator, who was blinded to treatment assignment and did not engage in discussion of adverse effects, rated the CGI-Improvement scale at each visit and the CYBOCS-ASD at baseline, Weeks 4 and 8. The CYBOCS-ASD includes a symptom checklist and five severity dimensions (Time Spent, Interference, Distress, Resistance and Degree of Control) each rated from 0 to 4 for a total score from 0 to 20.

Results: Using clinician-rated CYBOCS-ASD scores at baseline, Week 4 and Week 8, we compared the change on the CYBOCS across the four treatment groups (placebo and double-blind risperidone in Study 1, risperidone alone and risperidone plus parent training in Study 2) with a linear repeated measures mixed model. After eight weeks of treatment, CYBOCS-ASD total scores declined in the three active treatment groups, and showed no change with placebo. Pair-wise comparisons showed significant differences in the change from baseline to Week 8 between placebo and all active treatment groups: Study 1 blinded risperidone (effect size = 0.74); Study 2 risperidone alone (effect size=0.88) and Study 2 risperidone plus Parent Training (effect size = 0.86). There were no significant differences between any of the active treatment groups.

Conclusions: The CYBOCS-ASD is a reliable measure of repetitive behavior in children with ASD which is sensitive to treatment change and ready for use in clinical trials.

**123.154 154** Inflexible Behavior in ASD and Typically Developing Children in Age-Appropriate Play Activities. C. M. Whitehouse*[1], T. R. Vollmer[1], K. Radonovich[1], S. K. Slocum[1], K. P. Peters[2], C. L. Phillips[3], K. Burrichter[1], K. Wunderlich[1] and M. H. Lewis[1], (1)*University of Florida*, (2)*University of Florida Behavior Analysis Research Clinic*, (3)*John's Hopkins Hospital*

Background:

Restricted, repetitive behavior is a defining feature of ASD, and includes behaviors that reflect an insistence on sameness or resistance to change. Children with ASD often follow fixed routines, show unusual preoccupation with objects, exhibit intense, circumscribed interests, perseverate in use of language, and are intolerant of new situations. It is not clear, however, whether ASD children differ from typically developing (TD) children in how rigid or inflexible they are in engaging in age appropriate everyday activities. Generating clear evidence for such differences in ASD and TD children will provide a solid rationale for a shift in treatment to include attempts to increase general variability and flexibility in behavior. This study is part of a larger research agenda designed to address the core problem of rigid and inflexible behavior in ASD.

Objectives:

The primary aim of this study was to assess restricted inflexible behavior in ASD and TD children using direct observations of behavior in a standardized environment with age appropriate activities.

Methods:

Six activities were selected for two different age groups, younger children (ages 6-11 years old) and older children (ages 12-16 year old). Activities included computer time, watching a video, coloring, and other age appropriate activities. Participants included 19 ASD and 19 TD children matched on age, sex, and IQ. Participants were observed throughout two, 30-min sessions. In session one, children were told to play with any of the activities available. In session two, the same initial instruction was given and a prompt to switch activities was delivered if the subject was engaged with the same activity continuously for 2 minutes. Primary dependent measures included the number and duration of activities engaged with, transitions from one activity to another, and compliance to the prompts to switch. Additionally,

any measures of idiosyncratic motor and vocal repetitive behavior also were scored.

Results:

Two distinct response patterns emerged from the data. First, in session one, we found overall more variability in the number of activities and transitions in the TD children compared to the ASD group. As expected, however, there were a number of ASD children and TD children that demonstrated similar response patterns, which consisted of only engaging with one item throughout the entire 30-min session. The difference among was the two groups was most apparent in session 2. On average, the TD group made 18 activity transitions compared to an average of 10 transitions in the ASD group. The average compliance to the prompt to switch was 77% in the TD group and 28% in the ASD group.

Conclusions:

Though outcomes of session one appeared similar for many of the ASD and TD subjects, differences between the ASD and TD groups were most apparent in session two. Overall, the results demonstrated that restricted, inflexible behavior was characteristic of ASD children in interacting with play activities in a standardized environment. Moreover, transitions in these participants were limited even when prompted. These results represent the first such systematic comparison of observable inflexible behavior in ASD versus TD children.

## 124 Services

**124.155 155** Acceptability and Feasibility of Peer-Mediated Pivotal Response Treatment for Children with Autistic Spectrum Disorders: An Integrated Knowledge Translation Approach. A. Boudreau*[1], I. M. Smith[2] and M. Kerr[3], (1)*Dalhousie University*, (2)*Dalhousie University / IWK Health Centre*, (3)*Mount Saint Vincent University*

Background: The gap in effective intervention models for children with autistic spectrum disorders (ASD) at school is striking. The lack of evidence-based practices (EBPs) for children with ASD in schools may indicate inadequate translation of research into practice (Stahmer, Suhrheinrich, Reed, & Schreibman, 2012). This knowledge-to-practice gap frustrates researchers and educators alike (Dingfelder & Mandell, 2011; Stahmer et al., 2012). While researchers tend to focus on the fidelity of intervention implementation in lab settings, educators often feel that researchers do not consider the complexity of implementing interventions in the real-world school environment (Kasari & Parsons, 2013; Stahmer, Collings, & Palinka, 2005). Collaborating with knowledge users throughout the research process in an "integrated knowledge translation" (CIHR, 2006) framework may help to bridge the gap. Approaches in which typically developing peers are trained to implement an intervention directed toward children with a disability offer a logical, face-valid and cost-effective means of promoting social skill development for children with ASD. A specific peer training approach based on Pivotal Response Treatment (PRT; Koegel & Koegel, 2006) holds high heuristic value for implementation in schools given its emphasis on embedding learning opportunities into everyday contexts and routines (Koegel et al., 2011; Stahmer et al., 2011).

Objectives: The goal of the present study was to collaborate with a school board / school staff members and related stakeholders to develop a peer-mediated Pivotal Response Treatment (PRT) intervention targeting social skills for children with ASD in the first year of school. Feasibility of the proposed intervention in the school setting, as well as stakeholders' recommended modifications, were examined.

Methods: Semi-structured interviews were conducted with 24 educators and 5 early intervention providers ($N$=29) serving children with ASD. Qualitative methodology was used to obtain respondents' perspectives on EBP in general, components of the proposed intervention, and the overall acceptability and feasibility of implementing the intervention. Interviews were recorded, transcribed, and analyzed using grounded theory.

Results: Most participants had a rudimentary understanding of evidence-based intervention, but reported it to be important. Stakeholders' knowledge of PRT ranged from minimal to comprehensive. Overall, peer-mediated PRT was judged to be acceptable and feasible. Perceived strengths of the proposed intervention included: ecological validity, generalizability, potential for friendship development and greater acceptance of disabilities among classmates. Weaknesses identified included: sustainability of the model and uncertainty about how to train peers. Several

challenges with respect to peers as intervention agents and location of intervention were identified. Teachers recommended specific adaptations.

Conclusions: Findings highlight the added value of building a research-to-community partnership. Overall, stakeholders perceived peer-mediated PRT at school to be acceptable and feasible. A trial of the intervention is now proceeding. This process of obtaining qualitative feedback from frontline practitioners provides a model for researchers to promote EBPs for optimal classroom use. Findings are discussed within the framework of implementation science and effective and feasible models of ASD intervention at school.

**124.156 156** Access to Therapy for Children with Autism: A Population-Based Analysis. T. W. Benevides*[1], H. J. Carretta[2] and S. J. Lane[3], (1)*Thomas Jefferson University*, (2)*Florida State University*, (3)*Virginia Commonwealth University*

Background: Improving early access to effective care for children with autism spectrum disorder (ASD), while minimizing costs, is an important health policy objective. Occupational, physical, and speech-language therapy are frequently utilized non-behavioral services for children with an ASD (Thomas, Ellis, McLaurin & Morissey, 2007), and these services are utilized significantly more by children with ASD than by children with other special health care needs (SHCN) (Chiri & Warfield, 2012). Historically, disparities have been found in access to other services for children with ASD, particularly for underserved populations. However, existing research on therapy access is dated and studies were conducted prior to major policy and social changes that may impact access.

Objectives: The aim of this research was to examine population-based trends in access to therapy services for children with ASD under the age of 18 years, to compare differences in access to therapy services between children with ASD and children with SHCN, and to identify individual, family enabling, and need characteristics that contribute to reduced access to therapy services.

Methods: A retrospective, cross-sectional analysis using the 2005-06 and 2009-10 National Survey for Children with Special Health Care Needs (NS-CSHCN) was conducted. Weighted logistic regression models were used to examine access to therapy services at two time points for children with ASD between 3 and 18 years of age, and between children with other SHCN. NS-CSHCN datasets from the two time periods were concatenated after data cleaning to ensure appropriate merging of similar variables at both time points, and to ensure appropriate structure for use of imputed datasets (Blumberg et al., 2008). A series of nested logistic regression models were developed for analysis in Stata to control for the complex survey design and multiple imputation structure. The outcome variable was unmet need for therapy services, defined as children identified as needing therapy services in the past year, but who were reported to not receive all services in the past year (access variable). Predictor variables included diagnosis (ASD, SHCN), survey year, and a diagnosis by year interaction term, as well as models that included stepwise individual, enabling, and need characteristics that may be associated with unmet need for services.

Results: Results suggest that access rates were significantly poorer for children with ASD sampled in 2009 compared to 2005, with 24.7% (21.7-28.0, 95%CI) of children with ASD not receiving services in 2009 compared to 17.9% (15.0-21.3, 95%CI) of children with ASD not receiving services in 2005. Additionally, these rates of therapy access problems are significantly greater for children with ASD compared to children with other SHCN, with 12.8% (11.4-14.2, 95%CI) and 16.0 (14.6-17.5, 95%CI) of children with other SHCN not receiving needed therapy in 2005 and 2009 respectively. Additional analyses on groups with similar physical (e.g. fine/gross motor) and mental/behavioral need factors (e.g. socialization, behavior problems) will be described. Predisposing, family enabling, and need characteristics contributing to reduced access for children with ASD will be presented.

Conclusions: Results will be discussed in the context of potential policy implications and areas for future systemic interventions.

**124.157 157** Traits of Autism Spectrum Disorder and Co-Occurring Mental Health Problems Among Prisoners. H. L. Hayward*[1], L. Underwood[1], J. M. McCarthy[2], E. Chaplin[3] and D. G. Murphy[1], (1)*Institute of Psychiatry, King's College London*, (2)*St. Andrew's Healthcare Nottinghamshire*, (3)*Insititute of Psychiatry, King's College London*

Background:

The provision of support for people with autism spectrum disorder (ASD) within the community is improving as a consequence of policy and legislative changes. However, specialist services are not currently provided in prisons. Also recent initiatives to improve mental health care within the criminal justice system have not considered people with ASD. As a consequence, ASD and associated vulnerabilities including depression, anxiety and suicidality often go unrecognised and unsupported.

Objectives:

This aim of the study was to determine the extent of ASD and co-occurring mental health problems among prisoners. We tested the hypothesis that ASD traits would be unrecognised by prisons, and would be significantly associated with increased rates of anxiety, depression and suicidality.

Methods:

ASD traits were measured among 240 prisoners in a resettlement prison in London, UK using the 20-item Autism Quotient (AQ-20). Anxiety, depression and suicidality were assessed using the Mini International Neuropsychiatric Interview (MINI).

Results:

There were 39 participants (16%) with an AQ-20 score ≥10; indicating significant autistic traits. 12 prisoners (5%) were above research diagnostic cut off scores for ASD on the ADOS. Only three of these had been previously identified as having ASD. Mental health data were available for 37 'high autistic trait' participants and another 101 prisoners with no/low ASD traits. There was a significant positive association between AQ-20 and suicidality scores ($r$=.29, $p$=0.001). Participants with ASD traits had significantly higher suicidality scores (means=15.1 (ASD) vs. 5 (non-ASD), $p$= 0.001) and chi-square analysis showed that they were more likely to have a high suicidality rating (27% vs. 8 %), $p$=0.003) than those without ASD traits. Moreover, those with ASD were significantly more likely to be suffering from a current episode of depression (30% vs. 6%, $p$<0.001) or Generalised Anxiety Disorder (GAD) (27% vs. 11% $p$=0.019) and there were significant positive associations between AQ-20 and current depression ($r$=.43, $p$<0.001) and current GAD symptoms ($r$=.254, $p$=0.003).

Conclusions:

We identified high levels of unrecognised ASD traits among prisoners. Our initial data suggests that severity of ASD traits is a risk factor for suicidality and common mental health problems among prisoners. Improvements in prison health care should include improved recognition of ASD, and the detection (and appropriate treatment) of commonly occurring mental health symptoms.

**124.158 158** Availability of BCBA Providers As a Barrier to Service Implementation in ASD. R. P. Travis*[1], A. P. Juárez[2], C. R. Newsom[1] and Z. Warren[1], (1)*Vanderbilt University*, (2)*Vanderbilt Kennedy Center*

Background: According to the Centers for Disease Control and Prevention (CDC, 2012), an estimated 1 in 88 children and an estimated 1 out of 54 boys in the United States have an autism spectrum disorder (ASD). ASD is associated with enormous individual, familial, and societal costs across the lifespan (Amendah et al, 2011; Ganz, 2007). As such, effective early identification and treatment of ASD across resource-strained environments is often considered a public health emergency (IACC, 2012). Early, intensive ASD behavioral intervention embedding the principles of ABA is supported by several systematic and meta-analytic reviews (Reichow et al., 2012, Warren et al., 2011). While clinicians who specialize in the diagnosis and treatment of autism spectrum disorders often recommend behavioral services, there are numerous barriers to access of such services across diverse populations and geographies. While many parents report being able to implement educational and/or early intervention services (e.g., IEP development, speech therapy, occupational therapy), in some communities only a minority of families are able to implement recommendations regarding ABA-based intensive services (Warren et al., 2013).

Objectives: The current study examined availability of providers as a potential barrier to services.

Methods: Specifically, we examined the number of board-certified behavioral analysts across diverse geographies within the state of Tennessee in comparison to estimated numbers of children identified with ASD. This was done by county,

region, and on a state level and tied to examinations of geography (e.g., rural/ urban) and markers of income (SES).

Results: There are currently only 260 Board Certified Behavior Analysts (BCBA) registered in the state of Tennessee (Behavior Analyst Certification Board, 2013), which has a 2012 population estimate of 6,453,243 (US Census Bureau, 2013). Given an estimated annual life birth rate of approximately 88,000, some 1,000 children with ASD are born in TN on an annual basis. On a state level this translates into 260 BCBAs potentially available to serve 18,000 individuals under 18 with ASD and some 5000 individuals between 12-72 months of age. Several counties and zip codes did not have access to any BCBA providers with urban and insurance catchments having more access to providers.

Conclusions: Given the available number of BCBAs within our state, specific recommendations for early intensive services delivered or even supervised by BCBAs may not be realistic. This finding has both potent ethical and service system implications for clinical providers.

**124.159 159** Autism Speaks Early Access to Care Community Screening Event: Description and Preliminary Outcomes. L. M. Elder*[1], M. Chen[2], A. Halladay[1], A. M. M. Daniels[1] and P. Herrera[3], (1)*Autism Speaks*, (2)*UCLA*, (3)*211 LA*

**Background:** Autism Speaks Early Access to Care program seeks to reduce the average age of diagnosis and increase access to high-quality early intervention for all children on the autism spectrum. According to the CDC, the average age of diagnosis is 4-5 years, despite the ability to make a reliable autism diagnosis at 2 years. Studies have also documented that racial and ethnic minority populations and those of lower socioeconomic status are diagnosed later and less often. The earlier children are identified, the earlier they are able to receive early intervention services. Recent studies have attributed these disparities to differences in language, culture and awareness at both the family and provider levels. To address these challenges, Autism Speaks developed a free, community-based developmental screening program for underserved communities. The program includes partnerships with local expert clinicians, resources and community organizations.

**Objectives:** To describe the model and preliminary outcomes of Autism Speaks community screening event, delivered to an underserved community in Los Angeles on September 7th.

**Methods:** Families called in advance to schedule an appointment with expert clinicians. Walk-ins were taken as availability allowed. All families completed a developmental history form, the Parents' Evaluation of Developmental Status and the Communication and Symbolic Behavior Scales-Infant Toddler Checklist, Modified-Checklist for Autism in Toddlers, or the Social Communication Questionnaire, depending on the child's age. All families chose whether to complete the screening in English or Spanish. Clinicians met with the families for approximately 1 hour to provide feedback on developmental screening results, answer questions, and recommend follow-up services. Families then had the opportunity to visit a resource fair. Satisfaction was assessed using a five point scale, with 1 being very unsatisfied and 5 being very satisfied. Follow-up calls are being conducted by 2-1-1 LA (www.211LA.org) to ensure families successfully connect to local service providers.

**Results:** Seventy one children from 66 families were seen by a total of 24 clinicians. 83% of families spoke only Spanish and the average educational attainment was high school graduate. The average age of children seen was 5 years (range: 9 months – 13 years). 63% of children failed an autism-specific or social communication screener, and all parents indicated concerns on the PEDS. Among families completing the satisfaction scale (86%), mean scores ranged from 4.6 to 4.8 for the registration process, event day and appointment with clinicians. Mean overall satisfaction score for the event was 4.5 (*SD*=1.19).

**Conclusions:** Community-based screening events are successful at reaching underserved populations and can help lower the average age of an autism diagnosis. Parents found the event helpful and were highly satisfied with the services received. Follow-up data is also being collected on connection to services providers.

**124.160 160** Barriers to Care: An Investigation of Autism, Insurance, and Service Utilization. M. Mathew* and K. Koffer, *A.J. Drexel Autism Institute*

Background: Past research shows that the amount of covered services an individual with autism spectrum disorder (ASD) receives can vary based on health insurance type (Wang *et al.*, 2013). Coverage of care differs based on health insurance type and may encourage or deter people from seeking care. Therefore, it is necessary to study the impact of different health insurance types on services use among individuals with ASD. Barriers to care for individuals with ASD are especially pertinent to study because their quality of life can be increased through access to certain health services. By studying the impact of having public insurance, private insurance, or a combination of both on service utilization for individuals with ASD, recommendations for ameliorating barriers to care can be generated.

Objectives: This purpose of this study is to investigate how the service utilization of individuals with ASD is impacted based on their health insurance type. This research aims to predict the health insurance type driven barriers that individuals with ASD face in accessing the services needed to lead maximally independent lives.

Methods: The data for this research is from the 2009 Pennsylvania Autism Needs Assessment which contains survey results for 3,500+ individuals with ASD and their caregivers. This data contains variables that identify individuals' health insurance type and the services that they have accessed. Comparable proportions were used to obtain a "snapshot" of current service utilization. Linear regression models controlling for multiple factors including but not limited to race, ethnicity, income education status and sex, were designed to predict service utilization. The results from these regression models are forthcoming.

Results: Preliminary results show that depending on the service, it is variably advantageous to have public insurance, private insurance, or both. For neurology services, there was a greater percent utilization for individuals with private insurance (25.6%) compared to individuals with public insurance (19.0%). However, for services for sleep problems, individuals with public insurance had a greater percent utilization (25.7%) than individuals with private insurance (15.2%). Further research will be conducted to determine if any trends regarding service utilization are present.

Conclusions: Completed results of this study will be used to identify any barriers that exist for individuals with ASD in accessing services based on insurance type. Results will be used to craft policy recommendations to benefit individuals with ASD and their families and offer ways to increase access to services regardless of insurance status.

Wang, L. & Leslie, D.L. (2010). Health care expenditures for children with autism spectrum

disorders in Medicaid. *Journal of the American academy of child and adolescent psychiatry, 49* (11), 1165.

**124.161 161** Disparities in Utilization of Services Around the Time of Autism Spectrum Disorder Diagnosis. T. Savion-Lemieux*[1], M. Elsabbagh[2], M. Steiman[3], P. Szatmari[4], S. E. Bryson[5], E. Fombonne[6], T. Bennett[7], S. Georgiades[7], P. Mirenda[8], W. Roberts[4], I. M. Smith[9], T. Vaillancourt[10], J. Volden[11], C. Waddell[12], L. Zwaigenbaum[11], R. Bruno[13], E. K. Duku[7] and C. Shepherd[14], (1)*McGill University Health Centre-Research Institute*, (2)*McGill University*, (3)*The Montreal Children's Hospital*, (4)*University of Toronto*, (5)*Dalhousie/IWK Health Centre*, (6)*Oregon Health & Science University*, (7)*Offord Centre for Child Studies & McMaster University*, (8)*University of British Columbia*, (9)*Dalhousie University / IWK Health Centre*, (10)*University of Ottawa*, (11)*University of Alberta*, (12)*Simon Fraser University*, (13)*McGill University Health Centre - Research Institute*, (14)*Children's Health Policy Centre, Simon Fraser University*

**Background:** Many studies have pointed to the importance of early identification and treatment of ASD. However, despite mounting evidence, substantial delays still occur between the time of first expressed concerns, confirmation of diagnosis, and receipt of intervention services. It is well-documented that delays in diagnosis are related to geographic and sociodemographic factors. Fewer studies have examined variables influencing access to services around the time of diagnosis, which is critical for reducing the long-term impact of the condition.

**Objectives:** The present study examined disparities in utilization of services around the time of ASD diagnosis on the basis of family income across settings. We investigated the relationship between household income and service use in five regional referral centers across

Canada. Data were available through Pathways in ASD, a longitudinal study following preschoolers who received a diagnosis of ASD between ages 2 and 5 years in Halifax, Montreal, Hamilton, Edmonton, and Vancouver.

**Methods:** Parents completed a demographics survey and provided information about utilization/receipt of services; the latter information was coded using the Pathways Autism Services Log (PASL; Volden et al., in preparation) around the time of diagnosis. Data were available for 339 families. Overall, around the time of diagnosis, 17.5% of families in the national cohort were not receiving any services (either general community or specialized services). Information about demographics and service use was provided again 6 months later. To explore potential disparities in utilization (no services vs. any) on the basis of income, families were classified into three annual household income categories: lower (below $30,000 CAD), middle ($30,000-$80,000 CAD), and higher (above $80,000 CAD).

**Results:** There was a significant association between service use and income level (Chi-square = 13.8, p = .001, n= 339). Overall, 34.5% of lower income families were not receiving any services around the time of diagnosis vs.16.6% of middle- and 12.0% of higher-income families. We further inspected whether these disparities varied by site, given inter-provincial differences in service funding and delivery models. In three sites (Halifax, Vancouver, Edmonton), almost all families were receiving some service around the time of diagnosis. In the remaining sites, the association between income level and service use was mainly driven by the Montreal site (Chi-square = 12.3, p = 0.002, n= 123), which accounts for approximately a third of the overall national sample. In this site, 71.4% of lower-income families were not receiving any services around the time of diagnosis vs. 37.0% of middle-income and 27.1% of higher-income families. The disparities become narrower but do not completely close in the overall sample 6 months post-diagnosis, with 21.2% of families with lower income still not receiving services relative to 9.6% of middle- and 2.5% of higher income families.

**Conclusions:** These results highlight disparities in utilization of services around the time of diagnosis of ASD. Disparities appear to decrease over time, but do not disappear. This suggests that lower-income families experience more difficulty identifying, accessing, and/or sustaining services, with some regional differences noted. These findings have significant implications for regional/provincial policy makers and service providers.

**124.162 162** Closing the Gap Between Research Policy and Practice. C. Ramsden*[1], A. Roberts[1], M. Uljarevic[1], S. Carrington[2], L. J. White[2], L. Morgan[1] and S. R. Leekam[1], (1)*Cardiff University*, (2)*Wales Autism Research Centre*

Background:

Government policy and national practice guidelines have created an increasing need for autism services to adopt an evidence-based approach. However many practitioners and users of autism services are not aware of how to access and evaluate research evidence. At the same time, the impact of evidence produced by researchers often does not reach practice and policy. The overall goal was to create an on-line knowledge-sharing platform, the *Autism Research-Policy-Practice Hub* to close the gap between research, practice and policy and facilitate the co-production of knowledge. As translation of research into non-research communities raises many questions about how research knowledge will be accepted, understood and used, this study proceeded in several stages; focusing first on identifying stakeholder views about sharing of evidence-based research as reported here.

Objectives:

To determine the views of researchers and practitioner/policy professionals about (a) the extent of their engagement with each other (b) the main sources of knowledge that each group of professionals currently use, (c) the information and resources from research that they would like to be made available.

Methods:

Initial consultation and qualitative interviews led to an online survey targeting practitioners (in areas of clinical work, education and social care), policy workers (Government and third sector) and researchers. The survey was sent to UK professionals and two international email lists. There were 683 respondents; 422 researchers, 261 practitioners.

Results:

With respect to engagement between researchers and practitioners and/or policy workers, there was a difference in perception. While nearly half of the researchers stated that they engaged with non-academic professionals (practitioners and policy-workers) a lot or quite a bit, only a quarter of the non-academic professionals gave the same response. With respect to current knowledge, the practice and policy communities described their primary source of new knowledge as coming through attending training events, and from colleagues, while for researchers, the primary source of new knowledge is research articles. However, practitioners and researchers were in agreement about what would be needed to bring research more directly into practice. This included increased accessibility of research articles and practice-based guidelines which are based on reliable research and the ability to learn to apply research methods.

Conclusions:

Researchers depend on different knowledge sources (academic journals and research evidence) than practitioners and policy workers and have a different perception of their engagement with the non-academic community. However policy and practice communities are keen to engage with research, access research materials and learn to apply evidence-based research methods themselves. The results have been incorporated into the design and provision of resources now online in the Autism RPP Hub, http://www.autismrpphub.org. Further evaluation on useability and effectiveness of the hub is ongoing to enable adaptation to be made as the hub is used. We discuss the mismatch between the perception of researchers and non-researchers with respect to engagement with each other and consider evidence on the barriers to evidence-based practice in the field of autism.

**124.163 163** Development and Validation of a Psychosocial Quality of Life Questionnaire for Individuals with Neurodevelopmental Disorders. L. A. Markowitz*[1], C. Reyes[2], R. Embacher[1], L. L. Speer[1], N. J. Roizen[2] and T. W. Frazier[1], (1)*Cleveland Clinic Children's Hospital*, (2)*University Hospitals - Rainbow Babies & Children's Hospital*

Background: Quality of life (QoL) measures are important intervention and evaluation outcome factors when providing services to individuals with disabilities. Psychosocial QoL is particularly important for caregivers and families of individuals with autism and other developmental disabilities. Most of the existing QoL measures are geared toward physical illnesses or specific developmental conditions. There is a strong need for a measure that is applicable to a range of neurodevelopmental disorders. The Child and Family Quality of Life (CFQL) measure was developed to evaluate psychosocial QoL in neurodevelopmental disorder populations.

Objectives: The primary aim of this study was to psychometrically evaluate the CFQL to ensure high reliability of measurement. A secondary objective was to investigate differences in quality of life between children diagnosed with an Autism Spectrum Disorder (ASD) versus children with other developmental disabilities (non-ASD).

Methods: Caregivers of 212 individuals (ages 1-7) referred for concern of ASD completed the Child and Family Quality of Life (CFQL) instrument immediately before the first diagnostic assessment visit. The CFQL includes seven scales designed to measure different aspects of child and family QoL: child, family, caregiver, partner relationship, external support, financial, and coping. Scales were designed to be brief, easy-to-complete, and to generate specific clinical actions for scores suggestive of QoL impairment. Average item scores per scale range from 1-5, with scores ≤2 indicating low quality of life. Statistical analyses used to psychometrically evaluate the CFQL included: factor analyses to determine instrument structure, internal consistency reliability, and item response theory-derived reliability estimates across each scale's latent trait. Group comparisons (ASD vs. non-ASD) across CFQL scales examined whether QoL differed between ASD and non-ASD cases.

Results: Factor analyses identified six distinct, positively correlated, factors. Each of the original seven scales comprised a separate factor, with the exception that family and caregiver quality of life items had very high relationships and merged into a single factor in this young sample. Internal consistency reliability was good to excellent for these 4-5 item scales (α=.77-.97), with the exception of marginal reliability for coping (α=.67). Item response theory analyses demonstrated adequate to excellent measurement in the middle of each latent trait from 2SD to

+2SD (Reliability >.50), with adequate measurement down to -3SD (low QoL) for some scales. CFQL score distributions suggested highly variable QoL, with a non-trivial proportion of caregivers reporting low child, family, caregiver, and financial QoL (6.1% to 22.2% across scales) immediately prior to the diagnostic evaluation. Lastly, group comparisons found that caregivers of children with ASD reported significantly lower family quality of life (t(210)=2.15, p=.033; Cohen's d=.30) relative to caregivers of non-ASD children. Non-significant trends were also noted for child (p=.060), caregiver (p=.095), and partner relationship (p=.057).

Conclusions: Consistent with previous literature, a significant proportion of families affected by neurodevelopmental disorders report psychosocial QoL disturbance. Interventions are needed that address family QoL very soon after ASD diagnosis. The CFQL appears to be a useful clinical tool at the diagnostic stage for identifying QoL disruptions and developing clinical actions.

**124.164 164** Family Access to Disability Services: Is There Hope?. V. H. Mackintosh*[1] and B. Myers[2], (1)*University of Mary Washington*, (2)*Virginia Commonwealth University*

**Background:** Autism spectrum disorders (ASD) are an area of intense media focus. Many of these media stories have conflicting information as to what treatment approach can best address ASD. Parents might desire treatments for their children that are not available in their area, have long waiting lists, or are unaffordable. Interventions learned of on the internet may be unfamiliar to physicians and teachers, leading to conflicts with professionals. When reading anecdotal reports of a child recovering from autism due to an experimental approach, parents may struggle with passing up on *the* treatment that could help *their* child. If parents cannot find ways to meet their treatment goals for their children, this can leave them feeling hopeless.

**Objectives:** This study used a newly created measure, the *Family Access to Disability Services* (FADS) to explore parents' experiences with accessing desired services and how it relates to their feelings of hope.

**Methods:**

*Subjects:* This internet study included 280 parents of children with ASD (Autism, *n* = 134; Asperger's disorder, *n* = 36; & PDD-NOS, *n* = 42) or with Down syndrome (*n* = 68).

*Measures:*

The FADS is an 11-item measure that was created as part of a study exploring the process of choosing and providing therapies. Parents indicate the extent to which they agree/disagree with statements such as, "There are well trained professionals in our community to provide interventions for my child," "I feel like I have to meet many of my child's treatment needs myself" and "I feel like I need to educate the doctors and school personnel about my child's disability." Hope was measured using the State Hope Scale (Snyder, et al., 1996).

**Results:**

A one-way analysis of variance indicated that there were significant differences in FADS scores across the 4 diagnoses studied ($F$ (3, 252) = 8.21, $p$ < .001). Parents of children ASD diagnoses experienced more challenges accessing treatments than did parents of children with Down syndrome. There was no difference in the FADS scores within the ASD diagnoses.

The Family Access to Desired Services (FADS) measure correlated negatively with the hope measure, with more difficulty in accessing treatments relating to less hope. Hope scores correlated with diagnosis, with parents of children with Down syndrome reporting significantly higher levels of hope than parents of children with autism or PDD-NOS. Using a stepwise regression, a significant model emerged for predicting hopelessness. The Hope scores were predicted by diagnosis, family income, impairment level, and FADS. The total $R^2$ for the model was .26, with 14% of the variance in Hope scores explained by FADS measure after controlling for diagnosis, income and impairment level.

**Conclusions:** Using the new *Family Access to Disability Services (FADS)* measure, it was discovered that parents of children with an autism spectrum diagnosis had more difficulty than did parents of children with Down syndrome in accessing and providing the treatments they

wanted for their children. Higher *FADS* scores predicted less hope, even when first controlling for diagnosis, family income, and child's impairment level.

**124.165 165** Evaluating the Impact of Statewide Community-Based Training for Early Intervention Providers. L. V. Ibanez*, S. R. Edmunds, C. M. Harker, E. A. Karp and W. L. Stone, *University of Washington*

Background:

The Washington State ASAP! Program was designed to build capacity among birth-to-three providers to implement evidence-based screening and intervention practices with young children for whom ASD is suspected. Toward this end, free workshops offer training on the use of the Screening Tool for Autism in Toddlers (STAT) as a level 2 screener and the use of Reciprocal Imitation Training (RIT) as a low-cost, easily implementable, ASD specialized intervention. The present study reports on the preliminary effectiveness of RIT workshops and the acceptability of RIT for use by birth-to-three providers. RIT is a short-term, play-based behavioral intervention that uses a naturalistic approach to teach object and gesture imitation to children with ASD (Ingersoll, 2010).

Objectives:

To evaluate the effectiveness of RIT training workshops in increasing community providers' knowledge about, and implementation of, ASD-specialized early intervention.

Methods:

Four full-day RIT training workshops have been conducted to date in different areas of the state, and 150 service providers have attended. The majority of participants had backgrounds in either early childhood special education (44%) or speech-language pathology (19%), and their average number of years working with children with ASD was 4.94 (*SD*= 5.78). Workshops combine didactic presentations, group discussion, live demonstrations, and hands-on practice with performance-based feedback and coaching. Providers completed surveys assessing their knowledge, comfort working with young children with ASD, and implementation of RIT at 3 time points: before training, immediately after training, and 3 months following training. Survey items were rated on a scale from 1-4, with 4 indicating the most positive assessment or strongest agreement

Results:

Workshop evaluations revealed high levels of overall satisfaction (*M*= 3.7; *SD*=.29), with hands-on practice (21%) and video examples (35%) spontaneously listed by attendees as particular strengths. The percent of participants demonstrating mastery of RIT principles increased from 7% before training to 65% following the single-day training, $\chi^2$ (1)= 3.97, $p<.05$. Three-month follow-up surveys have been sent to 46 providers thus far, 21 of whom (46%) responded. Of the 19 responders currently working with children with ASD, 14 were using RIT and 5 indicated that they intend to start using RIT. Providers who were implementing RIT reported that RIT was effective in improving children's imitation skills (*M*= 3.5, *SD*=.52) and other social-communicative behaviors (*M*= 3.5, *SD*=.52). In addition, providers reported increased comfort from pre-training to 3-month post-training in providing direct intervention to young children with ASD, $t(16)= -3.04$, $p<.01$, coaching parents, $t(16)=-3.11$, $p<.01$, identifying treatment goals, $t(11)=-3.55$, $p<.01$, and discussing treatment goals with parents, $t(17)=-2.36$, $p<.05$.

Conclusions:

These preliminary results suggest that the ASAP! RIT workshops were well-received and resulted in increased knowledge about and use of RIT with families. Importantly, more generalized improvements were found in providers' comfort working with young children with ASD, coaching parents, and setting treatment goals. Data collection and follow-up assessments are continuing.

**124.166 166** Evaluation of a Multidisciplinary Parent Education Program on Families of Children Newly Diagnosed with Autism. K. V. Christodulu*, M. L. Rinaldi, K. S. Knapp-Ines and S. Fox, *University at Albany, SUNY*

Background: Research indicates that parents of children with autism spectrum disorders experience greater levels of stress than parents of typically developing children and even parents of children with other disabilities and chronic illness (Hassall et al., 2005; Tomanik et al., 2004). In

addition, parents of children with pervasive developmental disorders have been found to report a lower quality of life compared to parents of typically developing children (Mungo et al., 2007). Recent studies suggest that providing parents of young children with autism information about the diagnosis and effective treatment practices through parent education programs and support groups can decrease parenting stress (Keen et al., 2009; Tonge et al., 2006) and improve overall quality of life (Shu & Lung, 2005). The Center for Autism and Related Disabilities at the University at Albany, in collaboration with Capital*Care* Developmental Behavioral Pediatrics, developed an education program for parents of children newly diagnosed with autism. Training modules for the program were selected from topics recognized by the CDC, NIH, and Autism Speaks, as well as other leading organizations, as important for parents and families.

Objectives: Given the importance of families in the development, education, and behavioral support of children with autism, the purpose of this project is to increase parent knowledge, decrease parenting stress, and improve family quality of life in a timely manner using a format that is both efficient and effective.

Methods: Evaluation of the parent education program was conducted using reliable and valid tools. To assess level of parental stress, the Parenting Stress Index-Short Form (PSI-SF; Abidin, 1995) was given to parents. The Family Quality of Life Scale (FQOL; Summer et al., 2005) was used to gauge family life, and a test of general knowledge of autism was also administered. Each of these measures was completed by parents prior to and following participation in the education program. Additionally, a parent satisfaction survey was administered following completion of the program.

Results: Findings from 48 parents that have completed the project indicate that families of children recently diagnosed with autism are greatly benefitting from participation. Following the program, parents reported less overall stress. Specifically, parent stress scores on the PSI were in the elevated range prior to treatment but fell within normal limits following intervention. Parents also reported an improvement in quality of life following the program. Data showed positive changes on all subscales of the FQOL, with greatest change in the category of "emotional well-being" followed by "parenting" and "family interaction." Results also indicate that overall parents are highly satisfied with the program and following completion are more knowledgeable about autism.

Conclusions: Results of this project underscore the important role that working in partnership with parents play in improving outcomes. Making available to parents an education program that provides information on steps to take following a diagnosis of autism reduces likelihood that families will need to wait long periods of time before learning about and accessing resources for their child, leading to improved functioning for both child and family.

**124.167 167** Examination of Social Support and Stress Among Parents of Children with Autism Spectrum Disorder. L. C. Miller*[1], R. Hock[2] and M. E. Yingling[1], (1)*The University of South Carolina*, (2)*University of South Carolina*

Background: Parents of children with autism spectrum disorder (ASD) are often challenged by managing stress that can arise from behavior problems and social and communication deficits that typically developing children do not experience (Manning, Wainwright, & Bennett, 2010). Research indicates social support is a determinant of parental daily mood in parents of children with ASD (Pottie, Cohen, & Ingram, 2009) as well as increased well-being in parents of children with developmental disabilities (King, King, Rosenbaum, & Goffin, 1999). Findings have also indicated that stress and pressure from parenting a child with ASD can adversely affect marital relationships (Hock, Timm, & Ramisch, 2011). While demographic characteristics, including ethnicity, gender, and socioeconomic status, have been identified as determinants of perceived social support among the general population of adults in the United States (Almeida, Molnar, Kawachi, & Subramanian, 2009; Pugliesi, & Shook, 1998),little is known about the impact of race on perceived social support in parents of children with ASD. This study aims to evaluate race as a determinant of social support in the context of guidance, reassurance of worth, social integration, attachment, and reliable alliance among parents of children with ASD.

Objectives: This study had two objectives: 1) To determine whether African American and

Caucasian parents of children with ASD differ in perceptions of social support; and 2) To identify regression between social support and stress as it relates to adjustment of parents of children with ASD.

Methods: This study reports the findings of a cross-sectional survey of parents of children with ASD in a southeastern state. Participants included 252 parents of children with ASD. Participants were recruited via local treatment providers, ASD-specific listservs, support groups, and the SC Department of Disabilities and Special Needs (DDSN). The Parental Stress Scale (PSS) was used to measure parental stress and the Social Provisions Scale (SPS) was used to measure social support.

Results: Independent t-test was used to analyze results of the SPS and linear regression was used to analyze results of the PSS. T-test results indicated differences of perceived social support between Caucasian and African American parents were insignificant. Regression results indicated that the overall model of social support significantly predicts stress among Caucasian parents of children with ASD, R2=.218, F(1, 187)=54.16, p<.001. Elevated feelings of social support (β=-.467, p<.000) were associated with lower feelings of stress. Regression results also indicated that the overall model of social support significantly predicts stress among African American parents of children with ASD, R2=.276, F(1, 58)=22.11, p<.001. Elevated feelings of social support (β=-.525, p<.001) were associated with lower feelings of stress.

Conclusions: Having a thorough understanding of the relationship between stress and social support will allow the field of social science to develop more individualized services for parents of children with autism. Significant findings indicating higher levels of social support associating with lower levels of stress calls for future research to explore the aspects of social support which have the greatest influence on reducing stress.

**124.168 168** Parent Training in Pivotal Response Treatment: Bridging Disparity Among English- and Spanish-Speaking Families of Children with Autism Spectrum Disorder. N. L. Matthews*, B. Conti, C. Nuño and C. J. Smith, *Southwest Autism Research & Resource Center*

Background: Training parents to provide behavioral intervention can be a practical and cost effective treatment strategy. Little is known about effective training models for parents for whom Spanish is their primary language. Fidelity of implementation (FOI) is critical to success in parent training models (Coolican et al., 2010); thus, delineating the most effective method of training for this population is of importance. JumpStart is a parent education program conducted in both English and Spanish that includes brief parent training in pivotal response treatment (PRT) using guided observation of interventionist-child sessions.

Objectives: To compare the change in parent FOI among English JumpStart (EJS) and two models of Spanish JumpStart (SJS).

Methods: Participants were 46 parent-child dyads: 23 completed EJS (child: *M*age = 3.79, SD = 1.41; parent: *M*age = 34.03, SD = 6.81); 18 completed SJS-1 (child: *M*age = 3.88, SD = 0.98; parent: *M*age = 33.35, SD = 5.21), and 5 completed SJS-2 (child: *M*age = 4.48, SD = 1.58; parent: *M*age = 35.07, SD = 3.64). Children had an independent ASD diagnosis or at-risk classification. During SJS-1, intervention sessions were conducted in English and guided observation was conducted in Spanish. The guide needed to translate the interventionist-child interactions, which resulted in substantially fewer opportunities to explain PRT techniques. In SJS-2, intervention sessions were conducted in Spanish, allowing the guide to fully explain the PRT techniques. Videotaped 10-minute probes pre- and post-JumpStart completion were coded for overall parent FOI.

Results: Results of a 2x2 repeated measures ANOVA indicate that both EJS and SJS-1 groups demonstrated significant positive change in FOI from pre- to post-JumpStart [$F$ (1, 39) = 114.80, $p$ < .001]. However, a significant group by time interaction revealed that the EJS group demonstrated a larger positive change in FOI than the SJS-1 group [$F$ (1, 39) = 13.20, $p$ = .001]. When compared to change in FOI in the SJS-2 group ($M$ = 35.20%, $SD$ = 21.57), EJS parents demonstrated larger positive change ($M$ = 50.65%, $SD$ = 21.71) and SJS-1parents demonstrated smaller positive change ($M$ = 25.00%, $SD$= 23.35). Mann-Whitney U tests

revealed that these comparisons were not significant. ☐☐

Conclusions: Change in FOI was significantly lower among SJS-1 parents compared to EJS parents, indicating a need for more effective training techniques for Spanish speaking parents. Preliminary data from SJS-2 provide evidence for conducting both intervention and guided observation in Spanish. Although not statistically significant, SJS-2 parents demonstrated larger positive change in FOI than SJS-1 parents. Future examination of SJS-2 with a larger sample size may demonstrate a statistically significant benefit of this method. These findings support previously reported ethnic disparities in resource availability among families of children with ASD (Magana et al., 2012) and identify a potential method for reducing this disparity during training of parents for whom Spanish is their primary language.

**124.169 169** Parental Report of Familial Factors Influencing Emotional and Relational Functioning of Children with Autism Spectrum Disorder. K. L. Dykshoorn*, *University of Alberta*

Background: For children with Autism Spectrum Disorder (ASD), sibling relationships can be their primary peer influences. The connections and tensions in sibling relationship may impact the development, well-being and life quality that children with ASD experience. Evaluating how ASD affects sibling relationships is imperative, because positive sibling relationships lead to a higher quality of life presently and in the future, for both children (Beyer, 2009). Similarly, the caregiver's style affects both the sibling relationship and the development of each child (Doron & Sharabany, 2013). Williams et al. (2009) provide evidence supporting the positive impacts of authoritative parenting and the negative consequences of authoritarian parenting on the development of children. Further, despite best intentions, parenting stress can make parenting in an effective way difficult (Mills-Koonce et al., 2011) and caregivers raising a child with ASD often experience increased stress levels (Dabrowska & Pisula, 2010). Finally, the interplay between sibling relationships, caregiver characteristics, and success in ASD intervention is of interest.

Objectives: The integrated use of parenting habits and positive sibling relationships in promoting greater caregiver-perceived success in ASD intervention is worth evaluating and enhancing. The present study addressed the following variable associations: 1) parenting style and parenting stress impacting the sibling relationship; 2) sibling involvement in ASD intervention and success in ASD intervention strengthening the sibling relationship; and 3) parenting style, sibling involvement in ASD intervention and positive sibling relationships promoting greater degrees of success in ASD intervention.

Methods: Primary caregivers ($N$ = 108) completed an online questionnaire including: (1) the Sibling Relationship Questionnaire – Revised (Parent; Furman & Buhrmester, 1985); (2) the Parental Authority Questionnaire – Revised (Reitman, Rhode, Hupp, & Altobello, 2002); (3) the Parenting Stress Index – Short Form (Abidin, 1990); questionnaires developed by the author to evaluate (4) sibling involvement in ASD intervention and (5) parent-identified success in ASD intervention; and (6) a background questionnaire.

Results: Results indicated: 1) Parenting stress explains 12% of the variance found in the warmth and closeness of sibling relationships; 2) Sibling involvement and success in ASD intervention cumulatively contributes to 13.5% of the variance found in the warmth and closeness of sibling relationships; and 3) warmth and closeness uniquely explains 7% of the variance of success in ASD intervention.

Conclusions: The variances explained by the results of this study are significant and highlight the interconnectivity of factors contributing to children with ASD's success. Recognition of these relationships has important clinical significance, as it suggests an area of neglect in current practice with children with ASD. These areas will be discussed and clinical recommendations will be made. Enhancement of family well-being is important for each member of the family, including children with ASD. Theoretically, a shift from an individualistic framework to a systemic framework of ASD services and research is essential. Rather than focusing practice solely on the child with ASD, dedicating time to educating and assisting caregivers, understanding siblings and their needs, and promoting functioning and well-being for the children with ASD would be advantageous.

**124.171 171** Increasing Access to an Evidence-Based ASD Intervention Via a Telehealth Parent Training Program. A. Wainer* and B. Ingersoll, *Michigan State University*

Background: Systematic research focused on developing and improving strategies for the dissemination and implementation of evidence-based ASD services is essential. One nascent, yet promising, area of research has explored the use of telehealth programs to train parents of children with ASD in evidence-based intervention techniques. There are numerous benefits associated with the use of telehealth programs, including providing a cost-effective means for information to be accessed from anywhere at any time. The benefits of telehealth technology, together with the interest in such programs across health-related fields, and rapid increases in access to computer and internet technology for consumers, suggest that telehealth applications may serve as a promising alternative service-delivery model to increase the reach of, and access to, evidence-based ASD interventions, including ASD parent training programs.

Objectives: A hybrid telehealth program, combining self-directed internet-based instruction with remote coaching, was created to introduce parents of children with ASD to an evidence-based imitation intervention, Reciprocal imitation training (RIT). The first goal of the current study was to assess the degree to which parents could learn about and effectively implement RIT after engaging in the self-directed and coaching portions of the telehealth program. The second goal of the current study was to evaluate the impact of parent participation on child behavior, specifically spontaneous imitation skills. A final goal of the study was to assess the acceptability of this hybrid telehealth service delivery model to parents.

Methods: A single-subject multiple-baseline design study evaluated the effect of the program on changes in parent knowledge and behavior, and changes in child behavior, across 5 parent-child dyads. Participants engaged in a randomly assigned number of predetermined baseline sessions. Next, participants completed the self-directed portion of the program and then received three 30-minute remote coaching sessions from a parent trainer. One- and three-month follow up probes were also collected to examine maintenance of treatment effects. Changes in participant behavior were assessed throughout the four phases of the study (baseline, self-directed portion, remote coaching portion, and follow-up). Data examining the hybrid telehealth program's strengths and suggestions for improvement were collected.

Results: Program participation was associated with significant increases in parent knowledge about RIT and naturalistic intervention, and all parents demonstrated meaningful improvements in their abilities to correctly implement the intervention strategies in response to the program. Four out of the five children demonstrated clear increases in spontaneous imitation associated with parent participation in the hybrid telehealth program. Parents indicated that the intervention and hybrid telehealth service delivery model were acceptable, useable, and effective.

Conclusions: This study provides initial evidence for the effectiveness of a hybrid telehealth program in teaching parents evidence-based intervention strategies to improve spontaneous imitation in their young children with ASD. Results suggest that such hybrid telehealth programs may serve a role in significantly increasing access to evidence-based interventions for those on lengthy waitlists or living in areas with limited services.

**124.172 172** Influence of Child and Teacher Characteristics on Educational Placement of Students with Autism Spectrum Disorders. R. Aiello*[1] and L. A. Ruble[2], (1)*Vanderbilt University*, (2)*University of Kentucky*

Background:

Many professionals and families contend that inclusion of students with ASD in general education settings is the best approach to promote educational and overall progress in children with ASD. Others, however, harbor concerns about whether the inclusion model can meet the social and educational needs of children with ASD. Given the potential benefits and drawbacks of inclusive education, it is unclear how placement decisions are made for children with ASD. Few studies in particular have explored the links between educational placement and student characteristics. In general, these studies showed that children with higher IQ and milder forms of ASD were most likely to be placed in inclusive classrooms. External variables, such as teacher

characteristics, may also affect such placement decisions and warrant further exploration.

Objectives:

This project was undertaken to examine educational placement in a well-characterized sample of young children with ASD. The specific aims of the study were to examine child and teacher characteristics and the influence on educational placement.

Methods:

Forty-nine student-teacher dyads were recruited as part of a larger randomized controlled study on teacher consultation and coaching for young children with ASD between the ages of 3 and 8 years. Educational placement was determined by information obtained on IEPs along with the number of hours educated in the general education setting. A battery of baseline measures was completed to characterize the profiles of the students through direct assessment, including diagnostic, cognitive functioning, speech and language, and engagement in classroom setting. Caregiver report was also collected to determine behavioral functioning and adaptive functioning. Teachers were also asked to complete inventories for background and demographic information, stress, burn-out, administrative support, and self-efficacy.

Results:

Independent t-tests were conducted to compare child and teacher characteristics for general and special education settings. No significant differences for child or teacher characteristics across the two settings were obtained. Given that some students with ASD may not be entirely educated within only the general education or special education settings, a Pearson product-moment correlation was performed to determine the relationship between child and teacher characteristics and the number of hours spent in the general education setting as well as the number of minutes of more inclusive and restrictive supports. Main findings included moderate, positive correlations between hours of general education and cognitive functioning ($r$ = .32), communication ($r$ = .35), and age ($r$ = .33) along with a moderate, negative correlation for autism severity ($r$ = -.46). Teacher burn-out (emotional exhaustion $r$ = .43; depersonalization $r$ = .34; r = -.35) and self-efficacy ($r$ = .56) were also correlated with the number of minutes spent providing one-on-one instruction.

Conclusions:

As with previous studies, educational placement in inclusive settings was associated with higher cognitive functioning and speech abilities along with lesser symptomatology. The results also demonstrated a relationship between the beliefs teachers hold regarding their capability to bring about desired instructional outcomes and the burn-out experienced in high demand instructional situations.

**124.173 173** Multisensory Integration and Temporal Synchrony in Autism. E. Smith*[1], S. Zhang[2] and L. Bennetto[1], (1)*University of Rochester*, (2)*Stony Brook University School of Medicine*

Background: Multisensory integration is the process by which individuals combine information from multiple sources (e.g., vision, audition, touch) to produce a unique and unitary percept that produces a more accurate experience. Individuals with autism frequently show difficulty in multisensory integration tasks, and as a result may have difficulty locating and identifying stimuli in "noisy" sensory environments. This may be especially harmful during early development, when much of what is learned about language and communication depends on the ability to locate a speaker and identify what they are saying. A crucial aspect of multisensory integration in typical individuals is the ability to perceive and utilize temporal synchrony cues between two streams of information. Previous work strongly suggests that temporal synchrony detection may be altered in individuals with autism, but the effect of such a deficit on localization and identification of multisensory events has not been clearly studied.

Objectives: The present study examined the ability of individuals with autism to utilize temporal cues while locating and discriminating social and nonsocial audiovisual stimuli.

Methods: Twenty children and adolescents with high functioning autism and twenty well matched controls completed audiovisual localization and discrimination tasks presented with varying levels of audiovisual asynchrony. In Experiment 1, participants viewed side by side videos (of either a

person speaking or a ball bouncing), one of which matched the sound they heard and one of which was mismatched at varying levels of asynchrony. For Experiment 2, participants completed a discrimination task, in which they were asked to discriminate small differences in auditory stimuli during a social and nonsocial task. The videos for the stimuli were presented at varying levels of asynchrony and discrimination thresholds were determined for each level.

Results: Results from Experiment 1 revealed that individuals with autism showed a differential pattern of sensitivity to audiovisual asynchrony compared to controls when viewing social versus nonsocial stimuli. In particular, when using audiovisual synchrony to locate stimuli, individuals with autism showed a pattern of differentially larger Temporal Windows of Integration (TWI) for nonsocial compared to social stimuli in comparison to the pattern seen in the control group. However, results from Experiment 2 showed that individuals with autism showed enhanced auditory discrimination at baseline, and that they utilized temporal synchrony cues similarly to controls when discriminating audiovisual stimuli.

Conclusions: In combination, the results of this study place emphasis on the role of orientation and attention in audiovisual integration in autism, suggest differences in processing of social and nonsocial information, and show largely intact processing of temporal cues when task complexity is minimized. These results have implications for our theoretical understanding of the etiology of autism as well as expression and development of clinical symptoms.

**124.174 174** Stressful, Hopeful, and Strong Ecological Connections and the Well-Being of Parents of Adolescents with ASD. J. Kuhn*[1], K. Ehlers[1] and L. E. Smith[2], (1)*University of Wisconsin-Madison*, (2)*Waisman Center, University of Wisconsin-Madison*

Background:

Parents of children with autism spectrum disorder (ASD) experience poorer psychological well-being than parents with children without disabilities or parents other children with disabilities, including Down syndrome, cerebral palsy, and intellectual disability (Hayes & Watson, 2013; Abbeduto et al., 2004; Serrata, 2012). High levels of stress for families of children with ASD have been observed across the life course, with the adolescent period being a time of notably high stress. Much of the past research on the factors associated with stress and well-being has focused on child-related factors such as behavior problems and adaptive functioning. Less is known, however, about how environmental and system factors (e.g., interactions with formal systems and social networks) may impact family members' psychological well-being during the transition to adulthood.

Objectives:

The goal of the present study was to determine the extent to which different types of connections between ecological system levels (e.g., Bronfenbrenner, 1979), relate to the psychological well-being of parents of adolescents with ASD. Specifically, using an ecomap tool designed for use in clinical settings, we examined the impact of stressful, hopeful, and strong connections on parental negative affect, burden, and perceived stress.

Methods:

Participants (n = 25) were parents of adolescents (14-17 years of age) with ASD drawn from a larger, ongoing study of the *Transitioning Together* intervention, an 8-week education and support program for transition-aged youth with ASD and their families. Prior to beginning the intervention, parents completed ecomaps (i.e., a visual map reflecting the social ecology of the family). On the ecomap, lines were drawn to represent the type of connections (i.e., strong, stressful, hopeful) that participants described between themselves and various systems in their lives (e.g., child's school, medical providers). Ecomap responses were scored to provide the number of stressful, strong, and hopeful connections across and within ecological systems layers. Psychological well-being was measured with self-report measures including the Positive and Negative Affect Schedule (Watson et al., 1988), the Zarit Burden Interview (Zarit et al., 1980), and the Perceived Stress Scale (Cohen & Williamson, 1988). Associations among ecomap variables and measures of psychological well-being were examined.

Results:

We note that data collection is ongoing, with an anticipated final sample size of 50. Preliminary results indicated that a higher number of strong connections within the microsystem was associated with lower levels of parental perceived stress, $r$=-.56, $p$<.05. Stressful connections at each system level were significantly associated with higher levels of parental negative affect. Finally, a higher number of hopeful connections, specifically within the microsystem, was associated with higher levels of parental burden, $r$=.45, $p$< .10.

Conclusions:

Findings highlight the clinical and research utility of using an ecomap in this population as it can quickly assess multiple sources of stress and identify areas for resources and referrals. Increasing and enhancing family connections to microsystem level supports and services, such as respite, school that the child attends, etc., may be valuable target for intervention programming.

**124.175 175** Telescoping Health Disparities in Childhood Autism: Urban African American Families Providing Protection and Taking Action through Their Cultural Pain. K. W. Burkett*, *Cincinnati Children's Hospital Medical Center*

Background: Delays to the diagnosis and misdiagnosis of autism spectrum disorder (ASD) in African American children represent a considerable health care disparity in the United States. Untimely diagnosis and treatments in the care of African American children with ASD result in preventable delays in implementing interventions that improve outcomes. Cultural factors such as the child's presentation, clinician bias toward diagnosis of the European American child, access to health care for the African American child and cultural knowledge of ASD within the African American community have been implicated in the care disparities.

Objectives: The objective of this study was to discover the cultural care meanings, values, beliefs, practices and cultural ways of urban African American families caring for their child with autism.

Methods: An ethnonursing qualitative study was conducted to discover and systematically analyze meanings of care and cultural ways of urban African American families caring for their child with autism. Fifty two participants were interviewed and in-depth field observations conducted in their environmental context. Participants included 8 African American families with 24 family members of children with autism, and 28 health and school professionals. Data were analyzed and findings reported as they emerged from the patterns as themes.

Results: Two major culture care themes of providing protection and taking action for their child, underpinned by an additional finding of cultural pain, were significant to the health care disparities in diagnosis and treatment among African American children with ASD. The urban families provided protection by ensuring their child's independence in self-care, being watchful over their child's safety, and building trustworthy supports with health care and school professionals. They took action for their child as a means to balance choices for their child, family and community, to ease the stigma of disability and lack of cultural knowledge of ASD, and to address the ongoing challenges of poverty and inequitable education. The additional finding of cultural pain, defined as hurtful or offensive daily and nightly experiences, influenced the families' cultural ways as they sought to alleviate the cultural pain through humor, giving back and preparing their children for these experiences.

Conclusions: The findings substantiated that multiple cultural factors can influence the delays to diagnosis and treatment in the urban African American child with ASD. When clinicians provide culturally congruent care for African American families caring for their child with ASD through cultural awareness, building trustworthy relationships and reinforcing family strengths; there is the potential to mitigate some of the disparities in the health care of childhood ASD. Interventions are needed to address the systemic disparities in health care access and cultural knowledge of ASD within the African American community for urban African American families caring for children with ASD. Future directions are to employ community-based research methods in order to develop and test systemic interventions that impact the delays to diagnosis and treatment in African American children with ASD.

**124.176 176** Predictors of Child and Parent-Domain Stress Profiles in Parents of Children with Autism. T. M. Belkin*[1], J. H. McGrew[1] and L. A. Ruble[2], (1)*Indiana University- Purdue University Indianapolis*, (2)*University of Kentucky*

Background:

Parent caregivers of children with autism report greater levels of stress compared to parents of children with other developmental disabilities and parents of typically developing children (e.g., Baker-Ericzén et al., 2005; Yamada et al., 2007; Hayes & Watson, 2013). The transactional model of stress posits that stress is subjective and arises when demands placed on an individual exceed his or her resources to cope (Lazarus & Folkman, 1984). Consistent with this model, several "demand" and "resource" variables (e.g., challenging behaviors, child characteristics, and a lack of support) have been consistently associated with increased stress in caregivers of children with autism (Lecavalier & Wiltz, 2006; Mori et al., 2009; Pisula, 2011).

Objectives:

The current study expanded upon a previous investigation of parent stress within a sample of parents of children with autism by using a modified stress and coping framework (The Double ABCX model; McCubbin & Patterson, 1983a). We aimed to determine whether resource and demand antecedent variables would be associated with parent stress. Moreover, we examined stress separately within the Child Domain (i.e., Distractibility/Hyperactivity, Adaptability, Reinforces Parent, Demandingness, Mood, and Acceptability) and the Parent Domain (i.e., Competence, Isolation, Attachment, Health, Role Restriction, Depression, and Spouse/Parenting Partner Relationship) of the Parenting Stress Index: Fourth Edition (PSI-4; Abidin, 1985).

Methods:

As part of a prior randomized controlled trial study investigating the COMPASS intervention (Ruble et al., 2012), seventy-nine parents of children with autism were administered questionnaires and measures including the PSI-4 (Abidin, 1985).

Results:

Bivariate analyses indicated that parent-reported stress when measured within the child domain was significantly associated with eight variables: parental race, total services received, taking part in the COMPASS intervention, language, IQ, problem behaviors, adaptive behavior, and number of children in the home (all p values < .05). Parent stress when measured within the parent domain was significantly associated with six variables: mother's degree of education, parental race, income, total services received, parent-teacher alliance, and problem behaviors (all p values < .05). Parental race, total services received, and problem behaviors were significantly associated with increased reports of stress for both child- and parent-domain measures.

Multivariately, child-domain parental stress was related to problem behaviors ($\beta$ = .50) and participating in the COMPASS intervention ($\beta$ = -.32), accounting for 46% of the variance and parent-domain parental stress was related to behavioral symptoms ($\beta$ = .45), mother's education level ($\beta$ = -.38), and total number of services received ($\beta$ = .24), accounting for 45% of the variance.

Conclusions:

By organizing our study variables using a modified Double ABCX model, we were able to model factors associated with parent stress for caregivers of children with autism. Our findings are largely consistent with previous research and with theory that increased demands (e.g., challenging behaviors) lead to increased stress, and increased resources (e.g., mother's educational level or income) are stress protective (Estes et al., 2013; Lecavalier & Wiltz, 2006). Future research should examine specific moderators of stress to help understand and facilitate resilience within caregivers of individuals with autism (Hayes & Watson, 2013).

**124.177 177** Prospective Study of Families of Children with Autism Spectrum Disorder in the Emergency Department. A. Deavenport*[1], J. Semple-Hess[2], G. Yu[3], V. J. Wang[2] and L. Yin[2], (1)*Children's Hospital Los Angeles*, (2)*Children's Hospital Los Angeles/Keck School of Medicine of USC*, (3)*RAND*

Background: Children with autism spectrum disorders (ASD) may visit the emergency department (ED) more frequently compared to typically developing children. Despite experiencing multiple comorbidities, children with ASD are often discharged with diagnoses that could potentially be treated in primary care settings, but current research is limited.

Objectives: To understand the differences in ED utilization among children with ASD and other developmental disabilities (DD) compared to typically developing children.

Methods: A prospective cohort study was implemented in the ED at a level 1 pediatric trauma center in 2013. Children with ASD or other DD and those who were typically developing were followed as they were admitted in the ED. Main outcomes were the number of visits per child and whether hospitalization occurred.

Results: There were 353 children, 0-20 years of age, who visited the ED 1101 times; of these, the rate of visits was 4.7 among children with ASD or another DD, compared to 2.8 among typically developing children. The most common presenting "chief complaint" expressed by parents were similar among children with ASD or another DD and among typically developing children: trauma, infection, and abdominal pain. There were a total of 51 hospitalizations: 20.9% among children with ASD or another DD and 4.7% among typically developing children. The majority of children in all groups were covered by Medicaid and were of Hispanic descent. In all groups, having either ASD or another DD, being Hispanic ($\beta$=0.13 $t(280) = 2.1$, $p<0.05$), and having a lower age ($\beta$=-0.13, $t(280) = -2.31$, $p<0.05$), significantly predicted the number of visits. There were no significant differences in odds of hospitalization between children who had ASD or another DD and typically developing children.

Conclusions: High demand for ED care contributes to overcrowding, increased costs and fragmentation of care. Most families visited the ED for the same reasons. Children with ASD or another DD utilized the ED more frequently than typically developing children, however, they did not have greater odds of hospitalization. More research is needed to explore factors related to potential ED utilization, particularly among children with ASD or another DD.

**124.178 178** Psychiatric Diagnoses and Concordance with Clinician Diagnosis of Children with Autism Spectrum Disorders Served in Community Mental Health Settings. N. Stadnick*[1], C. Chlebowski[2], M. Baker-Ericzen[2] and L. Brookman-Frazee[2], (1)*San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology*, (2)*University of California, San Diego*

Background: Research suggests that discrepancies exist in child psychiatric diagnoses between those assigned by community mental health (CMH) therapists and those determined by standardized assessment tools (Haine et al., 2007; Lewczyk et al., 2003). Accurate classification of psychiatric co-morbidity is critical to determine diagnostic prevalence and inform development, implementation, and dissemination of evidence-based practices in CMH settings. Children with an autism spectrum disorder (ASD) are often served in CMH settings due to their high rates of co-occurring psychiatric disorders. Information on the types and diagnostic accuracy of co-occurring mental health problems is critical to bolster efforts to improve care for youth with ASD served in CMH settings.

Objectives: This study reports preliminary psychiatric diagnostic data from an ongoing randomized community effectiveness trial of AIM HI ("An Individualized Mental Health Intervention for ASD") conducted within publicly-funded community and school-based MH services. AIM HI is a clinical intervention targeting challenging behaviors in children with ASD and designed to be delivered by MH therapists. The prevalence of child diagnoses for children receiving community and school-based MH services are presented. Further, concordance between MH clinician-assigned diagnoses and those derived from an adapted MINI-KID (Sheehan et al., 1998), a structured diagnostic interview that corresponds with the DSM-IV, are reported.

Methods: The current sample includes 69 children (86% male, 52% Hispanic) ages 5-14 (M = 8.81; SD = 2.63) with an existing ASD diagnosis that was validated with the ADOS-II, and their primary caregivers. Children were drawn from 12 participating publicly-funded community and school MH programs, receiving care from 60 MH therapists. Four trained study personnel administered the MINI-KID to all caregivers. Prevalence data for diagnoses from the MINI-KID and clinician-report were analyzed using descriptive statistics, Chi-square analyses were used to compare differences in prevalence between clinician-assigned and MINI-KID diagnoses. Data from the MINI-KID were compared to clinician-report diagnoses by calculating Cohen's kappa statistic. The latter analyses were examined by four diagnostic

categories: ADHD, disruptive behavior disorder, mood, and anxiety.

Results: Approximately 90% of children met diagnostic criteria for at least one non-ASD diagnosis based on the MINI-KID. The most prevalent MINI-KID diagnoses were: ADHD (88%), a disruptive behavior disorder (57%), an anxiety disorder (49%), and a mood disorder (26%). There were no statistically significant differences in prevalence rates between clinician-assigned and MINI-KID diagnoses. Overall, diagnostic agreement between MINI-KID and clinician assigned diagnoses was poor and below the standard for moderate agreement beyond chance (Cohen, 1960). The κ values for ADHD was 0.07 (poor), 0.08 for disruptive behavior disorders (poor), 0.12 for anxiety (poor), and 0.15 for mood (poor).

Conclusions: Results suggest that diagnostic co-morbidity is high among children with ASD receiving MH services. Further, diagnostic concordance between clinician report and the MINI-KID was poor for this sample of school-aged children with ASD served in CMH settings. Additional analyses will be conducted to identify factors that may explain this poor diagnostic agreement. Preliminary results underscore the need for improved diagnostic evaluation to ultimately inform efforts to improve care for youth with ASD served in CMH settings.

**124.179 179** The Shotgun Approach or Acceptance: Parents' Treatment Selection for Children with ASD. B. E. Drouillard*[1], M. N. Gragg[1], R. T. Miceli[2], M. M. Ben-Aoun[1] and S. C. Popovic[1], (1)*University of Windsor*, (2)*St. Clair College*

Background: Coming to accept a child's ASD diagnosis is a difficult process which often continues many years after first receiving the news. With the importance of early intervention, however, parents often make important treatment decisions for their children before fully accepting the diagnosis. As such, it has been hypothesized that parents with low acceptance of their children's ASD diagnoses may be vulnerable to false claims made by empirically unsupported treatments.

Objectives: To explore the association between parents' acceptance of their children's ASD diagnoses and their treatment selection for their children with ASD. Parents' perspectives on the meaning of accepting the ASD diagnosis and factors influencing their acceptance will also be outlined.

Methods: One hundred twenty four parents (91.1% mothers; 79.8% White) of children with ASD (84.7% male; 74.2% White; *M* age = 8.83 years) completed an online survey composed of a demographic questionnaire (including treatments used), Acceptance and Action Questionnaire-II (Autism), and 10 open-ended items regarding their thoughts about ASD and treatments. Participants were most commonly between the ages of 35 and 44 (49.2%), from the United States or Canada (70.2%), married or in common-law relationships (80.6%), college/university graduates (75.8%), and had an annual household income of over $75 000 (46%). A subset of 10 parents also completed semi-structured telephone follow-up interviews regarding their conceptualizations of ASD, acceptance of their children's diagnoses, and experiences selecting treatments. Data were analyzed using correlational and thematic analyses.

Results: Quantitative results revealed that parents' acceptance of their children's ASD was significantly negatively correlated with the number of empirically unsupported treatments they selected for their children ($r$ = -.211, $p$ < .05, $R^2$ = 0.044), but was also significantly negatively correlated with the number of empirically supported treatments they selected for their children ($r$ = -.179, $p$ < .05, $R^2$ = 0.032). In other words, low levels of acceptance of children's ASD diagnoses were associated with a "shotgun approach" to treatment selection, whereby these parents selected more treatments for their children, regardless of empirical support. Qualitative results indicated that parents define acceptance of their children's ASD as: (a) having a balanced view of their children, (b) recognizing the children's potential, and (c) resolving their grieving/mourning process. They also noted the negative consequences of not accepting the ASD diagnosis. Parents reported that the factors influencing their acceptance of their children's ASD included: (a) community supports and barriers, (b) their knowledge of ASD, and (c) receiving the official diagnosis. A minority of parents also reported that, upon first recognizing the symptoms, they accepted the future diagnosis. Illustrative excerpts from parents' interviews will also be highlighted.

Conclusions: Parents with low acceptance of their children's ASD diagnoses often appear to take a "shotgun approach" to treatment selection. Professionals should maintain open dialogues with parents about the process of accepting the diagnosis, focusing on increasing ASD knowledge/community supports and reducing community barriers. Evidence-based interventions such as acceptance and commitment therapy may also lead parents to more selectively focus on empirically-supported interventions for their children with ASD.

**124.180 180** Socio-Demographic Variation in Parent Belief about the Causes of Learning and Developmental Problems Among Children with Autism Spectrum Disorder. K. Zuckerman*, O. J. Lindly, B. K. Sinche, P. D. Sidor and C. Nicolaidis, *Oregon Health & Science University*

Background: Causes of learning and developmental problems in autism spectrum disorder (ASD) are unclear; however, families' causal beliefs may be important in understanding health-seeking behaviors and health services utilization for ASD.

Objectives: The objective of this study was to assess socio-demographic differences in parent beliefs about the causes of learning and developmental problems in a nationally-representative survey of U.S. families of children with ASD.

Methods: Using data from the 2011 Survey of Pathways to Diagnosis and Services, we analyzed beliefs of 1420 parents of children with ASD. Survey items assessed whether parents felt the cause of child's learning and developmental condition was genetic or hereditary, was caused by an in-utero or post-natal exposure, or was affected by an accident, illness, or injury. We used bivariate and multivariate logistic regression to assess the associations of socio-demographic characteristics (age, gender, race/ethnicity, household income, health insurance status, U.S. region, functional limitations status, parent educational attainment, and family structure) with each parent belief.

Results: Beliefs about a genetic/hereditary cause of the child's condition were less likely among parents of boys (29.1% vs. 44.1% in girls; adjusted odds ratio [AOR]: 0.50 [0.30-0.82]) and parents of Latino children (17.2% vs. 34.6% in White non-Latino children; AOR: 0.21 [0.10 - 0.41]), and more likely among step-families compared to two-parent biological or adopted families (40.1% vs. 28.3%; AOR: 1.88 [1.06 - 3.32]). Beliefs about child's condition being caused by a post-natal exposure were more common in parents of Latino children (25.5% vs. 15.1% in White non-Latino children, AOR: 3.21 [1.33 - 7.75]) and parents of African-American children (35.5% vs. 15.1% in White non-Latino children; AOR: 2.40 [1.07 - 5.39]). Beliefs that an accident, illness, or injury had an effect on development were more likely in families living at <100% of U.S. Federal Poverty Level (64.4% vs. 49.5% in families living at >400% Federal Poverty Level; AOR: 3.48 [1.39-8.71]), and parents of children with functional limitations (61.1% vs. 50.6% of children without functional limitations; AOR: 1.78 [1.06-2.99]). There was no significant variation in parent beliefs according to child age, U.S. region, or child health insurance status.

Conclusions: In this nationally-representative sample of families affected by ASD, analyses suggested significant socio-demographic variation in parent beliefs. Parent beliefs about genetic/hereditary and exposure causes of children's conditions differed by gender race/ethnicity, and family structure. In addition, poverty and child functional limits were associated with differences in parent beliefs about accident or illness affecting the child's condition. Taking these beliefs into account may help providers in their conversations with diverse families. Further research is needed to assess how these beliefs modify health care quality or health services utilization.

**124.181 181** Who's Ready?: Predictors of Transition Planning for Adolescents with Autism Spectrum Disorder. J. Rankin*, M. Tudor and M. D. Lerner, *Stony Brook University*

Background: Transition Plans (TPs) are intended to help prepare adolescents with disabilities acquire specific skills that will aide them after high school. Despite the legal mandate for these services, as part of the Individualized Education Plan (IEP; Individuals with Disabilities Education Act, 2004), many youth may not have TPs. Extensive literature shows that adults with Autism Spectrum Disorder (ASD) tend to experience generally poor or limited outcomes after high school (e.g., Taylor & Seltzer, 2011), with higher functioning adolescents showing the starkest drop in improvements (e.g., Taylor & Seltzer, 2010); lack of TPs may be one reason for these poor

outcomes. Various factors have been proposed as related to TPs and outcomes for adolescents with ASD, including characteristics of the adolescent, the severity of their symptoms, and parenting factors (Hendricks & Wehman, 2009).
Examination of how such factors may predict the presence or absence of TPs, furthering the understanding of who may have TPs and who may not.

Objectives: The current study aims to identify a set of factors that may predict: 1) presence of Transition Assessments in the IEP, 2) presence of Transition Goals in the IEP, and 3) the presence of Transition-focused courses/services included in IEP. The following potential predictors will be examined: severity of ASD symptoms, age and gender, as well as parenting self-efficacy of their parents.

Methods: The parents of 26 adolescents with ASD (19 male; age range 11-22, $M$ = 15.5, $SD$ = 2.8) from a rural, underserved region, completed questionnaires prior to participation in a transition training group. Parents filled out a post-secondary transition checklist for families, the Social Responsiveness Scale (SRS) as a measure of ASD symptom severity, and the Parenting Self-Efficacy Scale (PSES) as a measure of parent self-efficacy. Three logistic regressions were conducted to test the impact of ASD severity, parental self-efficacy, and age on transition outcomes.

Results: In this sample, approximately half of the adolescents had TPs in their IEPs. Results indicated that older age predicted the presence of Transition Assessments ($p$ = .04) and presence of Transition Services/Courses present in adolescents IEPs ($p$ = .04). Lower PSES scores also predicted the presence of Transition Assessments on the IEP ($p$ = .01). Gender and ASD symptom severity were not evinced as significant predictors of any TP factors.

Conclusions: Results of this study indicate that age is a prominent predictor of the presence of Transition Assessments and Goals in the IEP of youth with ASD. This suggests a potentially problematic pattern in TPs for youth with ASD, wherein TPs become an IEP focus only when graduation is imminent, rather than based on individualized needs. Existing literature suggests that outcomes may be considerably better for youth with early TPs (e.g., Cobb & Alwell, 2009). Further, lower parenting self-efficacy predicted the presence of Transition Assessments, suggesting that parents with lower parenting self-efficacy are more inclined to seek out TPs through the school system.

**124.182 182** The Impact of Contact and Personality Traits on Attitudes Toward Individuals with Autism and Other Intellectual and Developmental Disabilities. J. DeSanctis*, L. Bennetto and R. D. Rogge, *University of Rochester*

Background: Changes in inclusive education and workplace integration have created a community that allows for more exposure and interaction between the general population and those with autism and other intellectual and developmental disabilities (IDD). With an increasing population of people with disabilities aging into adulthood, it is especially important to understand the impact of exposure and opportunities for interactions on attitudes toward these individuals, as the benefits of integration can often be attenuated by residual prejudice and discrimination. Previous studies have found that increased exposure can lead to more positive feelings toward those with IDD (Manetti, Schneider, & Siperstein, 2001; Piercy, Wilton, & Townsend, 2002). In other areas, studies examining quantity and quality of contact separately found that these two forms of contact may affect attitudes toward other groups in distinct ways (Voci & Hewstone, 2007; Islam & Hewstone, 1993). Additionally, studies have looked at personality dimensions as predictors of negative attitudes toward various minority groups, often finding that Agreeableness, Openness to Experience, and Social Dominance Orientation are related to attitudes (Sibley & Duckitt, 2008; Cohrs, Kämpfe-Hargrave, & Riemann, 2012).

Objectives: The current study further investigated attitudes by examining person by environment interactions between individual traits and types of contact with individuals with IDDs. We hoped to gain a better understanding of this relationship and to differentiate the effects of quality and quantity of contact when specifically considering lifetime exposure to people with an ASD or other IDDs. Better knowledge of this relationship will increase our understanding of possible barriers to inclusion and identify opportunities for program improvements.

Methods: In the present study, 550 adults completed a survey that measured their level of quantity and quality of contact with individuals

with IDD across their lifetime, personality factors, and their current attitudes. Our measure of attitudes captured feelings of exclusion, sheltering, and empowerment toward individuals with IDDs. The current study focused on exposure to individuals with IDDs broadly, as earlier diagnostic trends would likely influence adults' ability to differentiate between autism and other IDDs when recalling lifetime exposure.

Results: Multiple regression analyses suggested consistent links between higher quality of contact and lower levels of negative attitudes toward individuals with IDD (exclusion: **β**= -.332, p<001; empowerment: **β**=.391, p<001). The analyses further revealed significant person by environment interactions in shaping attitudes, and found that both agreeableness and social dominance moderated the impact of quality and quantity of contact on attitudes. Specifically, quality of contact was particularly beneficially associated with attitudes for people low on agreeableness or social dominance. In contrast, quantity of contact was detrimentally associated with attitudes for individuals high on social dominance.

Conclusions: These results suggest that mere exposure is not beneficial in decreasing negative attitudes and that contact that is meaningful and cooperative is related to more positive attitudes; this is especially important for individuals with certain personality traits. Recognizing the importance of quality of contact may be especially significant when designing and implementing inclusive opportunities for individuals with autism in our schools and general community.

**124.183 183** The Influence of Islamic Values on How Parents Face and Cope with a Family Diagnosis of Autism. J. Mahdi* and N. Madduri, *Vanderbilt University School of Medicine*

Background:

In traditionally Islamic countries, Autism Spectrum Disorder is often ignored and misunderstood. Accordingly, children with autism in these societies are sometimes ostracized despite the Islamic precedent that promotes their acceptance and respect. In this study, we examined the influence of Islamic values on the way autism is regarded and how it affects the way families perceive and raise their children as well as how children are integrated into their families and social and religious circles.

Objectives: The present study aims to evaluate issues that are encountered by families who follow Islam and have a child with ASD.

Methods: This IRB approved study consisted of qualitative interviews with Muslim parents with children with ASD from Texas and Tennessee. Topics discussed included parents' initial reaction to their child's diagnosis, current coping strategies, and religious, medical, and social problems the parents and their children faced.

Results: Even though faith served as a source of strength for parents and was emboldened upon taking care of their children, families were often isolated from their religious circles and extended families and met great intolerance as well as a lack of proper understanding and support from these communities.

Discussion: The themes found in traditionally Muslim societies also exist amongst others as well, reflecting the notion that even though Muslim families face discrimination from religious communities, it is not religion, but the cultural beliefs that have become intertwined with the religious community that underlie the isolation and lack of tolerance and acceptance of children with autism.

Conclusions: We hope these findings will lead to educational initiatives in mosques about children with ASD as well as the creation of religious support groups for parents.

**124.184 184** The Relationship Between Child Behaviors and Parent Feedback during a Problem-Solving Task. M. M. Pruitt*, L. Keylon and N. Ekas, *Texas Christian University*

Background: Parent-child interactions are important because they can have implications for the development of numerous skills, including social skills (Baker, Fenning, Cmic, Baker, & Blacher, 2007). It can be a stressful experience to parent a child with autism. Previous research suggests that increased symptom severity negatively impacts parent-child interactions (Beurkens, Hobson, & Hobson, 2013). One way parents interact with their child is through the feedback (e.g., praise) they provide. Feedback is a crucial element for a child's development, and it has been shown that one particular type of feedback, person-related praise (praise about stable attributes of a child), is related to negative feelings if failure later occurs (Brummelman,

Thomaes, Overbeek, Orobio de Castro, van den Hout, & Bushman, 2013). However, there are few studies of naturalistic praise in parent-child interactions with children with autism. Because previous studies have linked child behavior problems, parental stress, and parenting behavior (Hastings, 2002), it is important to examine how both symptom severity and behavior problems affect different dimensions of parenting.

Objectives: The current study utilized feedback as an example of one parenting behavior that may be impacted by children's symptom severity and behavior problems. Similar to studies examining other aspects of parenting behavior, we hypothesized that behavior problems would exhibit a stronger association with person-related praise

Methods: Seventeen participants from ages 3-6 with a diagnosis of autism completed a moderately difficult puzzle task with their parent's help. Observers coded feedback following a specific action on the puzzle as positive (i.e. praise), negative, or encouraging. This feedback was then classified as person-related, task-related, or ambiguous. Parents also completed the Social Responsiveness Scale (SRS) as a measure of symptom severity and the Behavior Assessment System for Children (BASC) as a measure of behavior problems.

Results: The results revealed a significant positive relationship between social cognition as measured by the SRS and person-related praise, $r = .49$, $p < .05$, In addition, there were significant positive relationships between person-related praise and child anxiety, $r = .78$, $p < .001$, and child depression, $r = .75$, $p \leq .001$, as measured by the BASC.

Conclusions: These results show that autism symptom severity, behavior problems, and parent-child interactions are related, confirming previous findings and extending them to another dimension of parent behaviors. The current data was collected at a single time point, which does not allow us to make directional conclusions. If person-related praise is predicted by child behaviors, our findings suggest that parent behaviors may be negatively impacted due to raising a child with autism. On the other hand, if person-related praise predicts anxiety and depression, it provides support for the contention that this type of feedback can have negative consequences for children with autism as well as typically developing children. We currently have two additional time points of data collected and intend to analyze longitudinal associations to determine the directionality of these effects.

**124.185 185** Understanding Child, Provider and Setting Characteristics That May Affect Fidelity of Implementation of Evidence-Based Practices. J. Suhrheinrich[1], T. Wang*[1], H. Lee[1], S. C. Roesch[2] and A. C. Stahmer[1], (1)*University of California San Diego*, (2)*San Diego State University*

Background:

The relationship between fidelity of implementation (FI) in community settings and child outcomes has become a critical issue as a demand for broader use of empirically supported behavioral treatments (ESBTs) increases. Most studies examine one type of FI, procedural fidelity (Odom et al., 2010), which measures the degree to which the provider uses procedures required to execute the treatment as intended. Another important type of FI is therapist competence (the level of skill and judgment used in executing the treatment; Schoenwald et al., 2011). Most studies examining FI of ESBTs do not account for these broader level variables, such as provider education, child characteristics, setting and competence, which may be just as important for child outcomes. There is thus a need to carefully evaluate relationships between these broader variables and behaviors targeted by ESBTs to develop an understanding of the necessary ingredients for effective community care.

Objectives:

To evaluate relationships between child behavior (within session) and provider demographics, child characteristics, setting and general therapeutic behavior in the context of implementation of a naturalistic behavioral intervention, Pivotal Response Training (PRT).

Methods:

As part of a larger investigation of key components of PRT, 296 video samples from archival data of research and community providers using PRT between 2000 and 2011 were reviewed. Demographics were collected for participating providers and children (age, race/ethnicity; provider education). Each video

unit was coded for specific child and adult behavior. Positive child behaviors included those associated with positive outcomes: active participation, functional object use, communication, and attention. Disruptive child behavior was also coded. Provider behaviors included those associated with good clinical skill: appropriate prompting, arrangement of the environment, presenting clear tasks, eliminating distractions, rapport, animation/affect, and management of unwanted behaviors. Videos were coded by trained, reliable coders who rated each element on a defined Likert scale. Hierarchical linear modeling (HLM) was used due to the nested structure of the data: (a) video units [level-1] nested within children [level-2] nested within providers [level-3]. Average disruption and average positive child behaviors were used as the target outcome variables.

Results:

Child race and age were significantly associated with disruptive behavior. White children had significantly higher average disruption scores and lower positive behavior scores than Asian and children of more than one race. Younger children had higher disruptive behavior than older children. Provider race was significantly associated with average positive behavior scores with Asian providers predicting significantly higher average positive child behavior scores over other races. On average, children in group settings (classrooms) had significantly lower positive behavior than children in one-to-one settings. Lack of variability in provider clinical skills limited our ability to conduct analyses on those variables. Additional fidelity data specific to PRT are currently being analyzed and will be presented.

Conclusions:

Provider, child and environmental characteristics may greatly affect child disruptive and positive behaviors within treatment sessions. These variables must be examined along with fidelity of implementation to help determine the effectiveness of evidence-based practices in community and research settings.

**124.186 186** Utilization of Various Treatment Types for Children and Adolescents with Autism Spectrum Disorder within the Simons Simplex Collection: Do Regional Differences Play a Role?. S. S. Mire*[1], K. P. Nowell[1] and R. P. Goin-Kochel[2], (1)*University of Houston*, (2)*Baylor College of Medicine*

Background: Children and adolescents with autism spectrum disorder (ASD) receive a variety of treatments. Yet treatments vary in empirical support (evidence-based versus negligible support), delivery setting (school-based versus private), and target (biochemical processes versus behavior and learning). Many factors, including family (e.g., parent educational attainment, family income) and child-specific (e.g., age, ASD severity, IQ) characteristics may associate with treatments pursued by families. Further, cultural norms within various geographic locales may influence treatment selection.

Objectives: The aim of the current study was to investigate factors (including geographic location) predicting use of treatment types.

Methods: Data were analyzed from children (*N*=2115, 86.3% male, *M* age=8.49 years) in the Simons Simplex Collection (SSC). Potential predictors of treatment use examined included parent education, family SES, child age, child IQ, and ASD symptom severity as indicated by the ADOS calibrated severity score (CSS). Treatment-history data were collected per parent report (recorded as either "current" or "ever" used) for each age, beginning at age 2. Nine treatment types were investigated: school-based speech therapy, school-based occupational therapy, private speech therapy, private occupational therapy, intensive behavioral, other intensive, biomedical, psychotropic medication, any other treatment, and no treatment. Logistic regression analyses predicted use/non-use of various treatment types. Regional differences were examined by comparing use of various treatment types in a local sub-sample (Baylor College of Medicine [BCM]; *N*=199) to the larger North American sample (*N*=2115) using chi-square analyses.

Results: Almost all families endorsed using some type of treatment (SSC: 95.6%, BCM: 93.1%; *M*=4 types). In both groups, school-based speech therapy was most often used (SSC: 80.4%, BCM: 73.0%). Separate tests of the full models (logistic regression) could reliably predict ($p<.001$) use or non-use of most treatment types. Older age, later ASD onset, and higher verbal-cognitive scores consistently were associated with lower likelihood of ever using various treatment types; higher parent-education and higher income were associated with greater likelihood of using various

treatment types. The SSC and BCM samples differed only on ethnicity, with a higher percentage of Hispanic/Latino participants in the BCM sample (26.1%) versus the SSC sample (10.9%). Chi-square analyses examining these two groups' ever having used various treatment types revealed significant differences for use of school-based OT ($c^2(2, 2372)=59.28$, $p<.001$), any other treatments (e.g., social skills) ($c^2(2, 2382)=50.52$, $p<.001$), and no treatment ($c^2=1514.59$, $p<.001$).

Conclusions: Overall, predictors of using various treatment types were similar between SSC and BCM participants but differed according to the type of treatment. Exceptions, however, included that BCM participants were significantly less likely to have school-based OT and "any other treatments" and significantly more likely to have no treatment. Investigating ways in which treatment use differs across the 12 North American-based SSC sites may assist professionals in identifying regions where certain treatment types are more/less widely adopted and exploring why such patterns occur. It is possible that differing demographic characteristics, such as higher representation of persons from Hispanic/Latino backgrounds, may contribute to differing patterns of treatment use in various regions and that these demographic factors are linked with cultural influences within their communities.

## 125 Specific Interventions - Pharmacologic

**125.187 187** A Pilot, Open-Label Study of Pregnenolone in the Treatment of Irritability in Autism Spectrum Disorder. L. K. Fung*[1], R. A. Libove[2] and A. Y. Hardan[2], (1)*Stanford University*, (2)*Stanford University School of Medicine*

Background:

One proposed model of autism suggests that the condition is a result of an altered ratio of excitation/inhibition in key neural systems. As GABAergic systems are the most important inhibitory neural pathways, modulators of $GABA_A$ receptors may correct the imbalance between excitation and inhibition in the brain. Pregnenolone is the precursor of GABAergic neurosteroids such as pregnenolone sulfate and allopregnanolone. We hypothesize that individuals with autism spectrum disorder (ASD) receiving pregnenolone will show reduction in disruptive behaviors as measured by standard rating scale for irritability.

Objectives:

(1) To conduct a pilot, open-label, 12-week trial to assess the effectiveness of pregnenolone in reducing irritability in adults with ASD. (2) To examine the safety and tolerability of pregnenolone in adults with ASD.

Methods:

This was a 12-week, prospective open-label study of pregnenolone in adults with ASD. Pregnenolone was initiated at a dose of 50 mg twice daily in weeks 1 and 2, then 100 mg twice daily in weeks 3 and 4, then 150 mg twice daily in weeks 5 and 6, then 200 mg twice daily in weeks 7 and 8, then 250 mg twice daily from weeks 9 to 12. If subjects could not tolerate a specific dose, s/he would be maintained at the highest tolerated dose. This initial phase was followed by a 4-week washout period to allow a better appreciation of the benefits observed while subjects were taking pregnenolone, by monitoring the effect of tapering and discontinuation of the medication. Primary outcome measure included the irritability subscale of the aberrant behavior checklist (ABC-I). Secondary measures included the other subscales of ABC, Social Responsiveness Scale (SRS), Sensory Profile Questionnaire (SPQ), and Vineland Adaptive Behavior Scale (VABS). In addition, vital signs and Dosage Record and Treatment Emergent Symptom Scale (DOTES) were monitored for adverse events. Paired, 2-tailed student t-tests were performed to compare outcome measures between baseline and 12 weeks.

Results:

Ten men and two women with ASD (mean age 22.5 ± 5.8 years; range 18.1-35.5 years; 9 Caucasians and 4 Asians) met the study criteria for inclusion in this open-label study. Pregnenolone yielded a statistically significant improvement in the primary measure, ABC-I [from 17.4 ± 7.4 at baseline to 11.2 ± 7.0 at 12 weeks ($p = 0.028$, $df = 11$, $t = 2.5$)]. Secondary measures were not statistically significant with the exception of ABC-lethargy ($p = 0.046$) and total SPQ score ($p = 0.009$). During the 12-week treatment period, two participants dropped out of the study. No significant vital sign changes occurred during this study. Pregnenolone was not associated with any severe side effects. Single

episodes of tiredness (n = 1), diarrhea (n = 1) and depressive affect (n =1) that could be related to pregnenolone were reported.

Conclusions:

Pregnenolone was modestly effective and well tolerated with participants with ASD in this pilot study. Further randomized controlled trials are warranted.

**125.188 188** The Effects of a Novel Vasopressin V1a Antagonist on Orienting to Biological Motion. F. Shic*[1], M. del Valle Rubido[2], E. Hollander[3], S. S. Jeste[4], J. T. McCracken[5], L. Scahill[6], O. Khwaja[7], L. Squassante[8], E. S. Kim[1], M. G. Perlmutter[1], E. Sharer[9], R. J. Jou[10], M. C. Lyons[10], T. Apelian[11], G. Berlin[3], C. J. Ferretti[12], A. Gavaletz[10], R. L. Loomis[13], T. Shimizu[14], B. P. Taylor[15], C. A. Wall[1] and D. Umbricht[16], (1)*Yale University School of Medicine*, (2)*Roche*, (3)*Albert Einstein College of Medicine*, (4)*UCLA*, (5)*UCLA Semel Institute for Neuroscience & Human Behavior*, (6)*Marcus Autism Center*, (7)*F.Hoffmann-La Roche AG*, (8)*F-Hoffmann-La Roche Ltd.*, (9)*Kennedy Krieger Insitiute*, (10)*Yale University*, (11)*UCLA Semel Institute CAN Clinic*, (12)*Montefiore Medical Center, Albert Einstein College of Medicine*, (13)*Yale University Child Study Center*, (14)*UCLA Center for Autism Research and Treatment*, (15)*Montefiore Medical Center/Albert Einstein College of Medicine*, (16)*F. Hoffmann - La Roche AG*

Background: Eye tracking has become an increasingly prominent tool in the study of ASDs. However, to date, only a few studies have used eye tracking to monitor the effects of potential interventions and no studies have used eye tracking to systematically evaluate the effects of novel pharmacological agents.

Objectives: To explore the impact of a novel V1a antagonist, RG4914, on the social attention of high-functioning adults with autism through eye-tracking tasks including biological motion preference.

Methods: High-functioning adults (M=23.4 years, range=18 to 40 years) with autism (n=19) participated in a multi-center (3-site), randomized, double-blind, placebo-controlled, cross-over study of the the effects of RG4914. Each participant was seen on two separate days for dosing. On the first dosing day, participants completed (1) predose assessments including eye tracking; (2) a 2 hour infusion of RG4914 or placebo; and (3) a postinfusion assessment battery including eye tracking. The second dosing day was similar to the first dosing day, with the exception of a crossover for the IV compound (RG4914 or placebo). Administered eye-tracking tasks included biological motion preference (based on work similar to Annaz et al., 2012). In this preference task, outcome variables included %Looking time towards the biological/social stimulus, %Orienting (% of trials where the first attended to stimulus was the more social target), and Latency (response time to attend to either the social or control stimulus).

Results: Linear mixed model analyses conducted over data aggregated for each eye-tracking task revealed a significant effect of RG4914 vs. placebo on %Orienting in biological motion preference tasks ($p<.05$, ES=0.8), with participants administered RG4914 directing their first gaze shift more often to biological motion targets. While similar analyses for Latency were not significant ($p>.05$), the effect size was moderate (ES=-.4) with trends suggesting that participants administered RG4914 orient more quickly as well as more often to biological information. Primary hypotheses on %Looking for biological motion preference were also not significant; however, an exploratory analysis revealed a significant interaction ($p=.05$) between the day of dosing and changes between pre- and post-infusion performance, with participants administered a placebo on day 1 showing greater decreases in looking at biological motion as compared to participants administered the active compound.

Conclusions: This study provides preliminary evidence of the ability of a novel V1a antagonist, RG4914, to affect behaviorally primitive and evolutionarily preserved attentional responses to biological motion. Furthermore, this study suggests that eye tracking may be useful not only for monitoring the effects of treatments for individuals with ASD, but may also serve as a valuable tool in the development of new interventions, behavioral, pharmacological, or otherwise. Because of the small sample sizes of this study, and the exploratory nature of both the analyses and the designed experiments, these results should be taken as preliminary.

**125.189 189** Effects of a Beta-Adrenergic Antagonist on Social and Cognitive Functioning in Autism Spectrum Disorder. R. M. Zamzow*[1], B. J. Ferguson[1], M. L. Lewis[1], A. S. Ragsdale[1], J. P. Stichter[2] and D. Q. Beversdorf[2], (1)*University of Missouri-Columbia*, (2)*University of Missouri*

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication impairments and restricted, repetitive behaviors. Current pharmacological interventions for ASD focus primarily on psychiatric symptoms, including agitation and obsessive behaviors. Few agents target core symptomatology, such as social and cognitive functioning. It has been previously hypothesized that stress contributes to social and cognitive deficits in ASD. Propranolol, a non-selective beta-adrenergic antagonist with known anxiolytic effects, is a potential therapeutic agent for ASD, as it blocks the noradrenergically mediated sympathetic response system. This agent has been previously reported to improve verbal fluency and working memory in ASD.

Objectives: The present study explores the effects of propranolol on performance on social and cognitive tasks in ASD. In addition, we sought to determine if those with higher baseline levels of sympathetic reactivity, measured by heart rate variability (HRV), exhibit the greatest response to propranolol, establishing a potential treatment response marker.

Methods: Twenty individuals with ASD participated in two study sessions, during which baseline HRV, assessed via electrocardiography, was measured for 5 minutes. Participants were then administered propranolol (40 mg) or placebo in a counterbalanced, double-blinded manner. 60 minutes following drug administration, participants performed several cognitive and social tasks. To assess social functioning, participants were given the Conversational Reciprocity component of the General Social Outcomes Measure (GSOM CR), in which participants engaged in a short conversation with the researcher. To assess verbal problem solving and verbal memory, the Anagrams task and the Hopkins Verbal Learning Test (HVLT) were administered.

Results: Paired samples *t*-tests revealed a significant improvement in the total score [$t(19) = 2.40$, $p = .03$] and the nonverbal communication score [$t(19) = 2.18$, $p = .04$] for the GSOM CR in the propranolol condition, as compared to the placebo condition. A trend for an increased sharing information score for this task in the propranolol condition was also observed [$t(19) = 1.76$, $p = .09$]. In addition, there was a significant decrease in the latency to correct response for the Anagrams task, in the propranolol condition, as compared to the placebo condition [$t(18) = 2.17$, $p = .045$]. Lastly, there was a trend for a between drug difference in the discrimination index for the HVLT, in which this score was higher in the propranolol condition [$t(19) = 1.80$, $p = .09$]. Simple linear regressions revealed a significant positive relationship between baseline HRV and response to propranolol for the GSOM CR total score [$F(1,18) = 5.38$, $p = .03$, $R^2 = .23$]. A trend for a positive relationship between baseline HRV and response to propranolol for the sharing information component of this task was also demonstrated [$F(1,18) = 3.11$, $p = .095$, $R^2 = .15$].

Conclusions: Propranolol appears to improve both social functioning and aspects of cognition in ASD. In addition, improvements in social functioning may be predicted by baseline sympathetic reactivity, where participants with greater heart rate variability demonstrate greater response to propranolol. Overall, these findings contribute to insight regarding potential therapeutic interventions for core symptomatology in ASD.

**125.190 190** Improving Outcome Measures for Rett Clinical Trials: The Development of Rett-Specific Anchors for the Clinical Global Impression Scales. N. E. Jones*[1], D. G. Glaze[2], J. L. Neul[2], M. Snape[3], E. Anagnostou[4] and J. Horrigan[1], (1)*Neuren Pharmaceuticals*, (2)*Baylor College of Medicine*, (3)*Autism Therapeutics Ltd*, (4)*Holland Bloorview Kids Rehabilitation Hospital*

**Background:** High quality outcome measures are a critical component to well-designed clinical trials for individuals with neurodevelopmental disorders. The Clinical Global Impression Scale (CGI) (Guy, 1976) is a measure of global clinical change with strong face validity that has been widely used as an outcome measure in CNS clinical trials, including trials in ASD. The CGI is a 7-point Likert rating scale that reflects expert clinical judgment. It includes a *severity of illness* (CGI-S) scale and an *improvement*(CGI-I) scale. Despite its favorable assay sensitivity in clinical trial settings, a disadvantage of the CGI is its lack of focus on the specific signs and symptoms of the disorder under study (Busner et al. 2009). Development of key anchors for the scale, specific to the disorder being assessed holds promise for enhancing the validity and reliability of the CGI for specific disorders.

**Objectives:** We describe the development of novel anchors specific to Rett syndrome (RTT) signs and symptoms for the CGI-I/CGI-S. This effort is part of an on-going clinical trial involving adolescent and adult females with RTT (ClinicalTrials.gov Identifier: NCT01703533), which is the first industry-sponsored, multi-site clinical trial in this population. RTT is a severe developmental disorder with features of ASD, and our experience using the CGI as an evaluation for RTT signs and symptoms may provide useful insights for the further development of anchors for ASD.

**Methods:** Utilizing information obtained from the RTT Natural History Study (ClinicalTrials.gov ID: NCT00299312), a classification grid of symptom severity was created, accompanied by anchors providing a description of progressive levels of impairment in core signs and symptoms.

**Results:** Based on score ranges from the RTT Natural History Clinical Severity Scale (CSS), a grid was developed defining gradations in the severity of the core signs and symptoms of RTT including: language/communication, ambulation, hand use, eye contact (social), autonomic function, seizures, and attentiveness. Each gradation was associated with a severity rating number from the CGI-S. For example, a CGI-S rating of 4 was associated with a CSS score range of 10-20. Specific exemplars from the grid were developed into descriptive anchors for the CGI, outlining signs and symptoms observed for each severity level. The anchors also provide descriptive guidance for differentiating ratings between CGI-S levels, when symptoms are not uniformly impaired across domains. For the CGI-I, anchors provide examples of symptom change as well as a framework for considering the duration, onset, durability of change, and context of symptom change across these domains.

24 of the targeted 48 study participants have been enrolled to date (mean age: 25 years, 10 months). Data presented from the full cohort will show the psychometric properties and feasibility of this RTT-specific version of the CGI scales in the context of this clinical trial.

**Conclusions:** The rating scheme captures clinically relevant gradations in severity and improvement of RTT-related signs and symptoms, offering the prospect of more consistent and relevant administration across research sites and studies, and it provides a framework for the further refinement of developmentally appropriate CGI anchors in ASD.

**125.191 191** The Effectiveness of Methylcobalamin and Folinic Acid Treatment on Adaptive Behavior in Children with Autistic Disorder. R. E. Frye*[1], S. Melnyk[2], G. J. Fuchs[3], T. Reid[2], S. L. Jernigan[1], O. Pavliv[2], A. S. Hubanks[2], D. Gaylor[2], L. Walters[2] and S. J. James[2], (1)*Arkansas Children's Hospital Research Institute*, (2)*University of Arkansas for Medical Sciences*, (3)*Arkansas Children's Hospital*

Background: Treatments targeting metabolic abnormalities in children with autism are limited. Previously we reported that a simple, safe and well-tolerated nutritional treatment with methylcobalamin and folinic acid significantly improved glutathione metabolism in children with autistic disorder who had evidence of low glutathione and methylation status.

Objectives: To determine whether treatment with methylcobalamin and folinic acid could improve adaptive behaviors in children with autism and abnormal glutathione and methylation metabolism and to determine whether such changes are related to alterations in glutathione metabolism.

Methods: Thirty-seven children diagnosed with autistic disorder (Diagnostic Statistical Manual Version 4 Text Revision and Childhood Autism Rating Scale) and abnormal glutathione metabolism (reduced-to-oxidized glutathione ratio < 6.0) and methylation metabolism (S-adenosylmethionine to S-adenosylhomocysteine ratio < 3.0) were treated with twice weekly 75µg/Kg methylcobalamin and twice daily 400µg folinic acid for 3 months in an open-label trial. The Vineland Adaptive Behavior Scale (VABS) and glutathione redox metabolites were measured at baseline and at the end of the treatment period.

Results: Over the treatment period, all VABS subscales significantly improved with most subscales demonstrating a medium-to-large effect size (average effect size of 0.59). Effect size for specific subscales were as follows: receptive (d=0.59), expressive (d=0.97) and written (d=0.56) communication skills, personal (d=0.65), domestic (d=0.37) and community (d=0.52) daily living skills and interpersonal (d=0.43), play-leisure (d=0.59) and coping (d=0.66) social skills. The average improvement in age-equivalent performance was 7.7 months

over the three month treatment period, with many subscales, particularly those with larger effect sizes, demonstrating large gains during the three-month intervention. This was particularly true for the communication domain where skills improved between 6.0 and 8.3 months, on average, and in the social skills domain where skills improved between 5.4 and 12.0 months, on average, over the three-month treatment period. The significant improvement in glutathione redox status was positively associated with an improvement in expressive communication, personal and domestic daily living skills and interpersonal, play-leisure and coping social skills. Age, gender and history of regression did not influence treatment response. The treatment was well-tolerated with no serious adverse effects although 14% of parents reported symptoms of moderate hyperactivity. Among the four children who dropped out of the study: two children dropped out because the parents were uncomfortable giving the methylcobalamin injections and 2 children dropped out because of hyperactivity and reduced sleep. Four families reported hyperactivity which resolved with decreasing the folinic acid dose to 400µg per day.

Conclusions: The significant adaptive behavioral improvements were observed and the positive relationship between behavior improvements and glutathione redox status suggests that nutritional interventions targeting redox metabolism may benefit some children with autism. Larger double-blind placebo controlled studies are needed to demonstrate the efficacy of this well-tolerated and safe treatment.

**125.192 192** The Efficacy of High-Dose Folinic Acid for Autism Spectrum Disorder: A Double-Blind Placebo Controlled Study. R. E. Frye*[1], J. C. Slattery[1], L. Delhey[2], M. Tippett[2], S. Melnyk[3], S. Rose[3], E. Quadros[4], J. M. Sequeira[4] and S. J. James[3], (1)*Arkansas Children's Hospital Research Institute*, (2)*ACHRI*, (3)*University of Arkansas for Medical Sciences*, (4)*SUNY Downstate*

Background: Autism spectrum disorder (ASD) is associated with several abnormalities of folate metabolism. Previous open-label studies have demonstrated that treatment with a high-dose reduced folate, folinic acid, at pharmacological doses, can improve language and behavior in ASD children. Folinic acid is believe to provide benefits since, as compared to other forms of folate, it can more readily enter the folate cycle and can be readily transported through the reduced folate carrier into the brain if folate receptor alpha autoantibodies are present. Previous research suggests that up to 75% of children with ASD have the presence of at least one of the two folate receptor alpha autoantibodies.

Objectives: To determine if high-dose folinic acid can improve language (primary outcome) and behavior (secondary outcome) in ASD children in a randomized double-blind placebo controlled trial.

Methods: Thirty-eight children with ASD (verified by the Autism Diagnostic Interview – Revised) and language impairment, without severe irritability (<=25 on the aberrant behavior checklist irritability score) who met inclusion and exclusion criteria were randomized to receive high-dose folinic acid (2mg/kg/day; maximum 50mg/day) in two divided daily doses or indistinguishable placebo capsules for 12-weeks. The dose was titrated up over 2 weeks to the target dose. At the beginning and end of the 12-week treatment period language and behavior were assessed. Language was assessed using the appropriate instrument given the child's age and language ability (preschool language scales or clinical evaluation of language fundamentals). Adaptive behavior was assessed using the Vineland adaptive behavior scale. Core and associated behavior was assessed using a combination of parental questionnaires (aberrant behavior checklist, social responsiveness scale) and clinician observation (Ohio autism clinic impression scale).

Results: Thirty-six children completed the study: one on active treatment could not comply with the treatment regimen because of an unforeseen family emergency and one on placebo was withdrawn from the study due to an adverse event that was unrelated to the study medication. Language scores increased significantly in the participants on folinic acid, whereas it remained unchanged for the participants receiving placebo ($p<0.005$) demonstrating that folinic acid significantly improved language (primary outcome). Raw scores for stereotyped behavior on the aberrant behavior checklist decreased significantly ($p<0.02$) for the group of participants receiving folinic acid as compared to the participants receiving placebo (secondary outcome). Several other measures of behavior on the Ohio autism clinic impression scale

demonstrated borderline significant trends towards improvement for the participants on folinic acid treatment as compared to the participants receiving placebo. The treatment was well-tolerated without any participants dropping out for any adverse events.

Conclusions: This double-blind placebo controlled study demonstrated the efficacy of high-dose folinic acid, a well-tolerated and safe treatment, for treating core and associated ASD symptoms, thereby confirming our previous open-label studies. Larger randomized multisite controlled trials are needed to confirm these preliminary findings.

### 126 Risk Assessment, Management and ASD

SIG Chair: Dr. Laurie Sperry Co-Chairs: Dr. Gary Mesibov, Dr. Todd Milford, Dr. Philip O'Donnell Our research group has worked collaboratively for 2 years and brings together scholars from the divergent fields of autism, forensic and clinical psychology, criminology, law, and education. Our focus is on the potential factors that predict increased risk for offending in people with ASD and management strategies to moderate those risks.

### 127 Approaching Adulthood: Transitional and Vocational Issues in ASD

SIG Co-Chairs: Dr. David Nicholas, University of Calgary, Canada; Dr. Lonnie Zwaigenbaum, University of Alberta, Canada Aims (1) To continue to facilitate networking for substantive priority planning and research development (2) To work toward specific research plans and galvanization of international networks for addressing gaps and opportunities for transitional and vocational research in ASD.

### 128 Technology and Autism

Chair: Sue Fletcher-Watson Committee: Gregory Abowd, Alyssa Alcorn, Renae Beaumont, Judith Good, Ouriel Grynszpan, Mari MacFarland, Helen Pain Technology and Autism: developing a framework for best practice in design, development, evaluation and dissemination of autism-specific technologies. The main issues raised at the 2013 SIG were: 1. the difficulty of appraising the volume and variety of technologies available for people with autism; 2. the lack of guidance for families and practitioners on how to use it; 3. the need for stronger research methodologies; 4. the need to share both data and technologies between researchers.

### 129 Global Knowledge Translation for Research on Early Identification and Intervention in Autism

Chairs: Mayada Elsabbagh and Petrus de Vries There is increasing appreciation of the need to enhance research impact through the iterative and dynamic process of knowledge translation: The synthesis, dissemination, exchange, and application of knowledge to improve quality of life for people affected by autism. This SIG will continue the dialogue on identifying knowledge gaps, barriers, and action priorities with a particular emphasis on global knowledge translation in the area of early identification and intervention for autism. The theme of this year's activities will be "To intervene or not to intervene: Effective and ethically sound application of evidence-based intervention models in diverse settings."

### 130 Keynote Address

Keynote Address - Friday

**130.001** Adolescents and Adults with ASD and their Families: Life Course Development and Bi-Directional Effects. M. R. Mailick*, *Waisman Center, University of Wisconsin-Madison*

### 131 Fundamental Processes in Cognition: Attention, Learning and Memory

*Organizer:* D. M. Bowler *City University London*

**131.001** The Intersection of Working Memory and Emotion Recognition in Autism Spectrum Disorders. S. A. Anderson*[1], D. Robins[2] and T. Z. King[2], (1)*University of Miami Miller School of Medicine*, (2)*Georgia State University*

Background: The executive functioning (EF) theory of autism spectrum disorders (ASD) grounds key impairments within the cognitive realm, whereas social-cognitive theories view social functioning impairments as primary. The current study examines aspects of both EF and social-cognitive functioning in ASD. Specifically, the focus is narrowed within EF to working memory (WM), operationalized with the *n*-back task. Many studies report deficits in verbal WM in ASD, whereas visual/spatial WM may be intact. EF based on emotion and motivation has been referred to as "hot" EF. Studies have examined WM using *n*-back for facial identity in ASD, but not for emotional expression; whereas, *n*-back for emotional expression has been investigated in controls, but not in ASD.

Objectives: The current study investigates "hot" executive function in ASD via, the *n*-back using emotionally expressive faces, as a model of social interaction. Hypotheses included less accuracy in ASD for 2- and 3-back conditions relative to controls in the context of similar 0 and 1 back performance. Reaction time for correct trials was analyzed for exploratory purposes.

Methods: The sample included young adults 17-30 years old with ASD ($N$=16, $N_{Males}$=11, $M_{age}$=21.63, $SD_{age}$=3.74 and a typically

developing sample matched on age ($N$=29, $N_{Males}$=2, $M_{age}$=20.34, $SD_{age}$=3.13). Stimuli consisted of cropped facial expressions (NimStim). Six basic emotions were balanced across all conditions. The 0-back served as baseline measure of short-term memory for emotional expression, followed by 1-, 2-, and 3-back tasks, 2 blocks each in pseudorandom order, counterbalanced within groups.

Results: Accuracy and reaction time were analyzed with 2 x 3 mixed ANOVA and post-hoc *t*-tests. Results demonstrated that the ASD group had significantly lower accuracy in 0-back, $t$ (19.562) = 3.564, $p$=.002, $d$=1, as well as in each WM load condition ($p$s<.001 to .007). There was no significant interaction between group and $n$-back level for accuracy. There was no main effect of group on reaction time. The effect of working memory load on reaction time was significant, $F$ (1.703, 3.56), $p$=.04, $\eta^2_{partial}$ = 0.076, with 1-back ($M$=76.30, $SD$= 10.66) significantly faster than 2-back ($M$=70.68, $SD$= 12.28) for the whole sample. The interaction term was significant and post-hoc within group analyses of changes in reaction time as working memory load increased revealed that the control group's reaction time significantly increased from 1- to 2-back, $F$ (1,28)=13.455, $p$=.001, $\eta^2_{partial}$=*.325*, whereas the ASD group's RT was not significantly different, $F$ (1, 15)= .784, $p$=.390, $\eta^2_{partial}$ =*.05*. Both ASD and control participants performed near chance on the 3-back (ASD accuracy 45-60%, control accuracy range 50-59%).

Conclusions:

The results suggest that the $n$-back with emotional expressions is too challenging at 3-back for both control and ASD populations. With limited exposure time, short-term memory for emotional expression is compromised in ASD, which is in contrast to previous findings of excellent short memory for facial expressions in controls. When visual stimuli include emotionally relevant information, working memory is deficient in ASD even at basic vigilance (0-back), despite evidence for intact visual/spatial working memory for non-social/non-emotional $n$-back stimuli.

**131.002** A Visual Perceptual Task Provides Evidence for an Excitatory:Inhibitory Imbalance in Adults with Autism. J. Horder*, M. A. Mendez, D. Spain, J. E. Faulkner, D. De La Harpe Golden and D. G. Murphy, *Institute of Psychiatry, King's College London*

Background: Sensory processing abnormalities are a key symptom of autism spectrum disorders (ASDs). In line with the emerging excitatory:inhibitory imbalance (E:I) hypothesis of ASD symptoms, it has been hypothesized that these sensory traits may be related to an imbalance in GABA and glutamate neurotransmission. However, this has not been directly tested in adults with an ASD..

Objectives: In order to investigate the functional balance between E:I neurotransmission in the visual cortex, we utilized the paradoxical motion perception task (PMPT). In this paradigm, high visual contrast normatively produces an impairment in perception of the direction of motion. This effect is referred to as paradoxical because, under most conditions, higher contrast stimuli are *easier* to perceive. The PMP effect reflects GABAergic lateral inhibition between neurons in visual cortex.

Methods: Medication-free adult males with ASD were recruited through a specialist clinic. All ASD participants were diagnosed using ADI-R and ADOS. Healthy control adult males were recruited via community advertisements. The two groups did not differ on age or full-scale IQ (t-test, p > 0.4). Participants age ranged from 18-56 years (mean 30.6) and IQ ranged from 95 to 139 (mean 119). Total n=30. During the PMPT, participants viewed vertical greyscale sine wave gratings of varying size (small vs. large) and contrast (bright vs. faint). On each trial, stimuli drifted either left or right at a constant speed. The task was to indicate the direction of motion, based on a brief presentation. The difficulty (duration of stimulus presentation) varied from trial to trial according to an adaptive 2-up-1-down staircase design with one staircase for each of the four stimulus conditions. In line with previous work, contrast impairment on motion perception is defined as the ratio between the estimated threshold (in milliseconds) for large-bright compared to large-faint stimuli.

Results: Adults with an ASD showed significantly reduced contrast-induced perceptual impairment (p=0.022, $t_{28}$ = 2.487). In other words, in the high contrast condition, individuals with an ASD selectively performed better than the controls. This effect was not accounted for by overall

difference in ability to perceive motion or to follow task instructions. Also, performance was not correlated with age (p=0.89) or IQ (p=0.2).

Conclusions: Adults with ASD have a selective enhancement of motion perception under conditions of high contrast. These data - the first results using this task in adults with ASD - are consistent with GABAergic abnormalities and an E:I imbalance model of the condition.

**131.003** Atypical Classical Conditioning in Children with Autism Spectrum Disorder. P. S. Powell*[1], L. G. Klinger[2], M. R. Klinger[1] and A. T. Meyer[2], (1)*University of North Carolina - Chapel Hill*, (2)*University of North Carolina*

Background:

Previous research examining classical conditioning in individuals with autism spectrum disorder (ASD) has indicated a pattern of both impaired (Gaigg & Bowler, 2007; South et al., 2013) and intact learning (Bernier et al., 2005; Sears et al., 1994; South et al., 2011). One explanation that may account for these findings is that individuals with ASD may acquire a conditioned response (CR) at a slower rate compared to individuals with typical development.

Objectives:

The primary objective of this study was to examine classical conditioning and the rate of acquisition (i.e., number of trials needed to demonstrate a conditioned response) in children with ASD compared to age and IQ matched children with typical development. Additionally, we examined whether differences in the rate of extinction were similar across both diagnostic groups.

Methods:

Nineteen children with ASD and 16 age and IQ matched children with typical development (age range: 8 to 14 years) participated in a classical conditioning paradigm (data collection ongoing). This task consisted of three phases (habituation, acquisition, and extinction). During the habituation phase participants were shown two different colored squares. During the acquisition phase one color (i.e., the conditioned stimulus; CS) was paired with a loud aversive sound (i.e., the unconditioned stimulus; UCS), with 100% reinforcement. Finally, during the extinction phase participants were shown four presentations of the CS without presentation of the loud noise. Participants' skin conductance responses (SCR's) were recorded throughout the task.

Results:

Our findings showed a significant increase in SCR to the CS compared to the neutral stimulus in both individuals with ASD and individuals with typical development, $F(1,32) = 13.94$, $p = .001$. However, despite similar overall group conditioning, a significant diagnosis (ASD vs. typical) by trial order (i.e., CS-UCS trial pairings) interaction was found, $F(1, 33) = 4.64$, $p = .04$. This finding showed that individuals with ASD needed a greater number of trials in order to learn the association between the CS and UCS. Analysis of CS trials during the extinction phase also revealed a significant diagnosis by pairing (CS vs. Neutral Stimulus) interaction, $F(1, 33) = 5.13$, $p = .03$, showing that individuals with ASD demonstrated a smaller CR compared to individuals with typical development after reinforcement was no longer provided (i.e., faster extinction).

Conclusions:

The present findings suggest that although individuals with ASD demonstrated a conditioned response, more trials were needed in order to demonstrate a reliable conditioned response that was similar to children with typical development. Analysis of the extinction phase also revealed that individuals with ASD were less likely to respond to the CS once reinforcement was no longer provided. These findings suggest not only a slower rate of associative learning in ASD, but also a greater likelihood of losing this learning once the reinforcement is no longer provided. Many theories of ASD suggest impairments in complex higher-order cognitive processes, however the present study demonstrates that the impairment in ASD may be a much more basic associative learning impairment which may underlie many cognitive impairments observed in this disorder.

**131.004** Enhanced Pattern Separation Memory in Adults Diagnosed with ASD. C. Nielson*, K. Stephenson, M. E. Maisel, A. R. Dorsett, M. South and C. B. Kirwan, *Brigham Young University*

Background: Jocelyne Bachevalier and others have demonstrated in non-human primates the

importance of tracking how specific timing and placement of lesions in the medial temporal lobe differentially affect autism symptoms. Behavioral studies by Bowler and colleagues have shown that atypical hippocampus function in ASD may underlie relational difficulties as well as some specific memory deficits. To date, however there have been few functional neuroimaging studies of explicit memory in ASD that can bridge these separate but converging lines of evidence. Memory tasks involving pattern separation can highlight mechanisms involved in interference reduction among similar memory representations and are important for memory accuracy. Pattern separation is thought to specifically involve dentate gyrus and CA3 regions of the hippocampus (Holden et al., 2013) that have been implicated in at least one mouse model of autism (Takeuchi et al., 2013).

Objectives: To characterize the neural correlates of performance on a pattern separation memory task in adults diagnosed with an ASD compared to age- and IQ-matched healthy controls.

Methods: While undergoing high-resolution fMRI scans, participants completed a continuous recognition task in which they were shown a series of everday objects one at a time. For each object, participants indicated whether it was new (a novel object that had never been seen), old (the exact same object had been seen before), or similar (similar, but not identical to one seen previously). The key comparison is the ability to identify "similar" but not identical objects.

Results: Participants diagnosed with ASD performed better than controls on the similar condition of the pattern separation task, indicating increased accuracy for detail overall. FMRI comparisons did not show significant differences in hippocampus activity but the ASD group showed some areas of greater prefrontal cortex activation during the similar condition, suggesting more effortful and/or more focused attention to the memory stimuli. This pattern is in line with other reports of better detail-oriented performance in high-functioning ASD and may contribute to difficulties tracking other complex stimuli, such as social interactions, because of extra neural resources devoted to lower-level tasks.

Conclusions: There is a need for more paradigms to investigate more specific brain regions—such as subregions of the hippocampus—in order to align human neuroimaging research with focused animal studies. Pattern separation tasks can offer such detailed investigations of the hippocampus including regions implicated in autism. These findings indicate that superior performance in some areas, such as memory for details, involves a cost in neural activity that may contribute to performance deficits in complex situations such as social interactions.

**131.005** Examining the Link Between Declarative Memory and Structural Language Ability in Children with Autism Spectrum Disorder (ASD). S. Anns*, J. Boucher, D. M. Bowler and S. B. Gaigg, *City University London*

**Background**:

It is well known that ASD is associated with a heterogeneous pattern of structural language ability that ranges from severe impairments in some individuals to superior skills in others. Yet the sources of this heterogeneity are unknown. Here we test the predictions that the language and learning impairments that distinguish low functioning autism (LFA) from high-functioning autism (HFA) most commonly result from an impairment of semantic memory additional to the impairment of episodic memory known to occur in all forms of ASD. More specifically, we hypothesize that whereas episodic memory (critically dependent on recollection) is impaired across the spectrum, semantic memory (critically dependent on familiarity) is impaired only in individuals with LFA. We also predict that impairments in semantic memory will correlate with lexical-semantic ability in children with LFA, when other relevant factors are controlled for.

**Objectives**:

The objective is to test specific predictions concerning the pattern of memory impairment in HFA and LFA and their relation to structural language ability in these groups (specifically lexical semantic knowledge).

**Methods**:

*Study 1*tested familiarity and recollection in 24 children (6-10 years) with HFA (VIQ>90), and 22 adolescents (11-17 years) with LFA (VIQ<75) using a shape recognition task and an action

recall source memory task. Two comparison groups were included: a young typically developing (TD) group of 43 children (6-10 years) and a group of 21 intellectually disabled adolescents (11-17 years) without autism (ID), equated with the LFA group for age and ability.

*Study 2* tested familiarity and recollection with the same participants as *Study 1*using forced choice recognition tests developed by Migo, Mayes et al. (2009) that discriminate between the processes of familiarity and recollection.

Participants also completed tests of lexical-semantic knowledge including the Pyramids and Palm Trees test and the Similarities and Vocabulary subtests from the Wechsler Abbreviated Scales of Intelligence. Of interest were not only group differences on the various dependant variables but also the relation between indices of familiarity and recollection and lexical semantic knowledge, whilst controlling for factors such as non-verbal IQ, mentalising ability, weak central coherence, and social economic status.

**Results**:

Results replicate earlier observations of impaired recollection but preserved familiarity in HFA compared to TD groups; but the LFA participants were surprisingly unimpaired compared to all other groups on the indices of familiarity. Interestingly the LFA group was superior on tests of weak central coherence and performance on this task correlated significantly with measures of familiarity and recollection particularly in this group. Moreover, we observed striking group differences in the pattern of correlations between lexical semantic knowledge and familiarity in both LFA and HFA groups but not in the ID or TD groups.

**Conclusions**:

LFAs' superior visual perceptual skills may compensate for impaired familiarity in tests of visual-spatial memory, as used here. Lexical semantic knowledge may emerge through fundamentally different routes in LFA, ID, and HFA, each building on whatever cognitive resources are available. These findings serve to highlight the different pattern of cognitive ability in intellectual disability, with and without autism.

**131.006** The Effect of Visual Perceptual Load on Auditory Awareness in Autism Spectrum Disorder. J. Tillmann*, A. Olguin, L. Gilmour and J. Swettenham, *University College London*

Background: This study investigated cross-modal selective attention in individuals with Autism Spectrum Disorders (ASD) by applying Lavie's Load theory of attention and cognitive control (Lavie, 2005). Load theory asserts that the extent to which task-irrelevant stimuli are processed depends on the level of perceptual load of the task (e.g. subtle (high load) vs. gross (low load) line discrimination). Previous results demonstrated that when visual perceptual load increases, adults with ASD continue to process task-irrelevant visual stimuli whereas control participants do not. These findings may reflect an increased perceptual capacity in ASD (Remington et al., 2009, 2012; Swettenham et al, in press). Perceptual load has also recently been identified as a critical factor in cross-modal selective attention in neurotypical adults using an "inattentional deafness" paradigm (Macdonald & Lavie, 2011). Awareness rates for an unexpected and task-irrelevant auditory stimulus on a critical trial were significantly reduced under high visual load compared to low visual load.

Objectives: The present study examined, for the first time, the effect of visual perceptual load on awareness of an auditory stimulus in children with ASD.

Methods: 26 children diagnosed with ASD (Mean age 10y 4m) and 44 typically developing children (TD) (Mean age 10y 2m), matched for chronological age and non-verbal IQ (Raven's), took part in the study. All participants were checked for normal or corrected-to-normal vision and normal hearing. The task was adapted from Macdonald & Lavie (2011) and involved participants judging which line of a briefly presented cross (110ms) was longest (horizontal vs. vertical). Participants were randomly assigned to either the high load (subtle line discrimination) or low load condition (gross discrimination). On the critical 7$^{th}$ trial, an unexpected, task-irrelevant auditory stimulus was played concurrently with the visual stimulus. Participants were then asked whether they had noticed anything else on that trial. On a subsequent control trial, participants were told to ignore the cross stimulus. Only those participants who successfully identified the auditory stimulus on the control trial and made

correct line judgments on at least 5 out of 7 trials (including the critical trial), were included in further analyses.

Results: As predicted by load theory, TD children were more likely to notice the auditory stimulus in the low visual load vs. high visual load task, $x^2$ (1) = 7.747, p = .005. This was not the case however for children with ASD, who demonstrated similar detection rates across perceptual load conditions, $x^2$ (1) = 0.016, p = .899, yet reported greater awareness than controls in the high perceptual load condition, $x^2$(1) = 8.474, p = .004.

Conclusions: Awareness rates for an auditory stimulus were reduced for TD controls under high visual perceptual load, but remained unaffected in children with ASD. These findings extend the hypothesis that individuals with ASD have an increased perceptual capacity to contexts involving cross modal selective attention.

**131.007** Inhibitory Mechanisms Underlying Vibrotactile Perception Appear Altered in Children with ASD. N. A. Puts*[1], E. L. Wodka[1], T. Koriakin[1], M. Tommerdahl[2], R. A. Edden[1] and S. H. Mostofsky[3], (1)*Kennedy Krieger Institute*, (2)*University of North Carolina*, (3)*Johns Hopkins School of Medicine*

Background:

Impaired responses to tactile stimulation are commonly reported in children with Autism Spectrum Disorder (ASD), and inabilities to habituate to sensory experiences and impairments in filtering (ir)-relevant sensory input have both been described. It has been hypothesised that disrupted neuronal inhibition underlies these sensory impairments and disrupted GABAergic function has been linked to autism. Recently we have shown that different aspects of tactile inhibitory function, including its role in habituation and filtering, can be probed using a battery of behavioral tasks. In this study we applied a battery of ten tasks to typically developing children (TDC) and children with ASD (ASD) to investigate the role of inhibition in the primary sensory cortex in different aspects of tactile processing in to investigate atypical touch sensitivity in ASD.

Objectives:

Test whether TDC and ASD pediatric populations differ in their response to tactile stimuli, and whether this is specific to tasks probing mechanisms related to habituation and filtering.

Methods:

*Participants*: 68 TDC and 32 children diagnosed with ASD (ages 8-12) participated (13F, 2 left-handed). Subject and parental consent was obtained under the approval of the IRB at Johns Hopkins University and the Kennedy Krieger Institute.

*Design:* All participants received a battery of vibrotactile tasks; (1) two reaction time tasks; (2) a static and dynamic (dynamic increase in amplitude) detection threshold (DT) task. (3) Two amplitude discrimination tasks (no adaptation, single site adaptation); (4) Sequential and simultaneous frequency discrimination; (5) Temporal Order Judgement (TOJ) with and without 25 Hz concurrent stimulation. All tasks used stepwise tracking and were preceded by three practice trials for training purposes.

Results:

There were no differences in reaction time (RT) between the groups, although individual variability in RT was higher in ASD ($p < 0.001$). Dynamic DT was significantly higher than static DT in TDC ($p < 0.008$), but not in ASD, and static DT was higher in ASD than TDC ($p < 0.005$). Amplitude discrimination increased after single-site adaptation compared to baseline amplitude discrimination in the TDC group ($p < 0.001$), but not in the ASD group ($p > 0.5$), but the unadapted condition was significantly worse for ASD ($p = 0.01$). There were no significant differences in frequency discrimination or TOJ performance between the tasks and groups.

Conclusions:

We have shown that children with ASD have different responses to vibrotactile stimulation than TDC. Differences in the effect of dynamic stimulation on detection threshold suggest impaired feed-forward inhibition in autism, which may reflect poor sensory filtering in autism. Higher baseline amplitude discrimination threshold in ASD compared to TDC, suggests that lateral inhibitory connections are weaker in ASD, and an absence of the effect of adaptation (as seen in TDC) suggests impaired modulation of lateral inhibitory connections in ASD, which may

reflect aberrant habituation. Intact frequency and temporal order discrimination suggest intact temporal and synchronous processing in ASD. Understanding the specific mechanisms underlying sensory symptoms in autism may allow for more specific therapeutic or drug-targeting in the near future, that may alleviate these symptoms and improve quality-of-life.

## 132 Early Development I

*Organizer:* L. Zwaigenbaum *University of Alberta*

**132.001** Correspondence Between Parent Report and Clinician Observation at 12 Months in Infants at High Risk for ASD. S. Macari*[1], D. J. Campbell[1], G. M. Chen[2], J. Koller[3] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Christian Academy in Japan*, (3)*Yale Child Study Center*

**Background:** Given the current emphasis on early screening for autism spectrum disorders (ASD), it is crucial to examine the efficacy of screening tools and understand the potential vulnerabilities associated with utilizing parent reports. Although parents have an optimal perspective from which to observe and engage with their infants across diverse contexts, utility of parent ratings in a high-risk population is unclear, given contrast effects based on an older sibling with ASD along with other limitations of informant reporting. To further the development of ASD screening tools for infants, it is critical to evaluate concordance between parent report and clinical observation.

**Objectives:** To investigate agreement across parental and clinician ratings, we compared similar items on the First Year Inventory (FYI; Baranek et al., 2003) a parent questionnaire designed to screen for ASD at 12 months, and the ADOS-Toddler (ADOS-T; Lord et al., 2013), a standardized ASD diagnostic tool, administered concurrently to 12-month-olds at high and low risk for ASD.

**Methods:** 161 (high-risk(HR)=95, low-risk(LR)=66) infants were evaluated with the ADOS-T at 12 months by clinicians blind to their risk status. Prior to the ADOS-T assessment, parents completed the FYI. Nine items describing comparable behaviors were identified across the instruments, including social, communication, and repetitive behavior. Each measure rates behaviors on a 0 to 3 scale. Items were compared using paired-samples t-tests with Bonferroni correction for multiple comparisons.

**Results:** Regardless of risk status, parents rated three speech and communication-related items (amount of babbling, directed vocalizations, and gestures) and object imitation as more typical compared to the clinical assessment ($p<.005$). Clinicians and parents in both risk groups agreed on items assessing response to name, response to joint attention, showing, and repetitive behaviors. Interestingly, response to name appeared twice on the FYI in slightly different formats. When the question was phrased globally (i.e., "Does your child answer to his name?"), both HR and LR parents rated the infant's behavior as more typical than the clinician ($p<.001$); however, when the same question was presented in a multiple-choice format ("What do you typically have to do to get your baby to turn towards you?"), parent and clinician ratings were more similar in both risk groups.

**Conclusions:** Parents of high- and low-risk infants rated their children's behaviors similarly to clinicians on a number of items tapping into social and repetitive behavior, but discrepancies between expert clinicians and parent ratings on speech and communication items were common in both risk groups and may reflect the effect of unfamiliar context on child's behavior during direct assessment. Wording of questions appeared to affect the degree of discrepancy between clinician and parent report. These findings suggest a further need to examine the sources of disagreement between parental report and clinician rating of key behaviors as well as the impact of design features on screening instruments' ability to capture behavior most accurately. In addition to these issues, our discussion will also include preliminary results of the FYI's utility in identifying those with a later ASD diagnosis in a high-risk sample.

**132.002** Parent Report of Onset Status: Prospective Versus Retrospective Methods. S. Ozonoff*[1], A. M. Iosif[2], G. S. S. Young[1] and M. Miller[1], (1)*UC Davis MIND Institute*, (2)*University of California at Davis*

Background: Previous studies have demonstrated that parent report of ASD onset status (regression, no regression) is limited and often does not agree with home video evidence (Ozonoff et al 2011) or longitudinal evaluations of behavior in the laboratory setting (Ozonoff et al 2010). Earlier studies often mixed methodologies, comparing prospective data with retrospective

parent report. It is therefore difficult to determine whether the poor concordance is due to limitations in parent recall or to differences in data collection methods.

Objectives: 1) To collect both prospective and retrospective parent ratings of their child's development, and 2) to compare parent ratings to longitudinal expert clinician judgments.

Methods: Using a prospective longitudinal design, infants at risk for ASD were seen at 6, 9, 12, 15, 18, 24, and 36 months of age. At each visit, both parents and clinicians rated the child's social-communicative development. At 36 months, parents were interviewed retrospectively with the Autism Diagnostic Interview-Revised (ADI-R) about any loss of skills. Data from all infants with an ASD outcome at 36 months are included in this analysis (n=20). Latent class analysis (LCA) was used to derive onset trajectories for the parent prospective ratings and the clinician longitudinal ratings. Kappa statistics and percent agreement among the methods were calculated.

Results: The LCA of the clinician ratings demonstrated two trajectories, one with initially low social-communication ratings that were stable over time (i.e., early onset trajectory; 10% of the sample) and one with initially high ratings that declined over time (i.e., regression trajectory; 90% of the sample). The LCA of the parent prospective ratings also demonstrated these two trajectories, with 70% of the sample classified on the regression trajectory. Parent and examiner ratings agreed with each other 60% of the time. In contrast, parent retrospective ratings agreed with their own prospective ratings only 30% of the time (kappa = -0.21; NS) and with clinician ratings only 30% of the time (kappa = -0.06; NS). In all cases, when regression was reported retrospectively by parents on the ADI-R, it was corroborated by prospective ratings (either parent, clinician, or both).

Conclusions: 1) The vast majority of infants who develop ASD demonstrate a regression or declining trajectory of social-communication development, according to prospectively collected data, whether rated by clinicians (90%) or parents (70%). 2) Parents have difficulty reporting on regression retrospectively. Far fewer parents report declining trajectories when asked retrospectively (30%) than prospectively (70%) and their retrospective report contradicts their own prospective report 70% of the time. However, when regression is reported on a retrospective instrument, it is corroborated by prospective data. 3) Obtaining parent ratings of development at well-child pediatric visits, and looking for declines in ratings from previous reports, may be useful as a screening method to help identify children who are developing ASD.

**132.004** Validation of the Modified Checklist for Autism in Toddlers-Revised with Follow-up (M-CHAT-R/F). D. L. L. Robins*[1], K. A. Casagrande[1], M. L. Barton[2], C. M. A. Chen[2], T. Dumont-Mathieu[2] and D. A. Fein[2], (1)*Georgia State University*, (2)*University of Connecticut*

Background: Early detection and early intervention for children with Autism Spectrum Disorder (ASD) improve outcomes. Because receiving effective intervention depends on the child being detected and diagnosed, early screening is crucial. The M-CHAT is one of the most widely used screening tools, but left room for improvement in its psychometric properties.

Objectives: Validate the 2-stage Modified Checklist for Autism in Toddlers, Revised, with Follow-up (M-CHAT-R/F) in a low-risk sample.

Methods: The M-CHAT was revised by eliminating three items, rearranging items to avoid positive response bias, simplifying language, and providing developmentally-appropriate examples. Children ($n$=16,115) were screened during 18- and 24-month well-child care visits in metro-Atlanta and Connecticut. Parents of at-risk cases completed the Follow-up with researchers by telephone. Children who continued to show risk for ASD were invited for a free diagnostic evaluation. In addition, missed cases were identified by physician flag for ASD concerns and secondary play-based screening.

Results: 92.6% of children screened negative; of those who completed the Follow-up, 63.2% no longer showed ASD risk . Of the 348 cases that continued to show risk for ASD, 221 attended evaluations; 105 were diagnosed with ASD, 104 were diagnosed with other developmental delays/concerns, and 12 were typically developing. The optimal scoring algorithm, determined by receiver operating characteristic curves was based on total score (area under the curve=.907): Children whose total score was 0-2 were low-risk, and no further assessment was

needed. Children whose total score was 3-7 required administration of the Follow-up, which clarified responses and elicited examples for at-risk responses; Follow-up scores of 2 or more warranted evaluation. Children whose initial score was 8 or higher can bypass Follow-up and be referred immediately for evaluation. The M-CHAT-R/F identified 105 cases of ASD; an additional 18 cases were identified based on other strategies. Sensitivity has an upper bound of .85, specificity=.99. Positive predictive value (PPV) for ASD was .48, and PPV for any developmental disorder/concern was .95. Likelihood ratio for positive screens was 114.05. Physician concerns identified 24% of ASD cases. Direct comparison between M-CHAT-R and original M-CHAT indicated that the rate of ASD detection increased (67/10,000 vs 45/10,000; $p$=.003) while the overall screen positive rate decreased from 9.15% to 7.17% ($\boldsymbol{X}^2$ (1, $n$=35,060)=39.62, $p$<.001).

Conclusions: The M-CHAT-R/F is a valid tool to screen for ASD during toddler check-ups. The questionnaire demonstrates improvements compared to the original M-CHAT, and has strong psychometric properties. Although the 2-stage screener identifies many children who do not have ASD, 95% of children who screen positive on the M-CHAT-R/F require evaluation to identify specific early intervention needs. The M-CHAT-R/F identified many more children with ASD than physicians' clinical judgment of ASD risk (105 vs. 30); however, physicians identified nine ASD cases missed by the M-CHAT-R/F. Also, although physicians were asked to indicate ASD risk, some did not follow this procedure consistently and may not have indicated risk if the screener was clearly positive. Therefore, the combination of surveillance and screening is likely to be the most powerful method for detecting ASD in toddlers.

**132.005** Observed Social Communication Profiles and Parent-Reported Red Flags of ASD in Toddlers with and without Autism Spectrum Disorder from Three Racial/Ethnic Groups.

S. Stronach*[1] and A. M. Wetherby[2], (1)*University of Minnesota - Twin Cities*, (2)*Florida State University Autism Institute*

Background: Racial and ethnic diversity is rapidly growing in the United States, leading to heightened concerns about racial/ethnic disparities in the provision of services for young toddlers with autism spectrum disorder (ASD). Studies have demonstrated that non-Hispanic White students with ASD are approximately two times more likely to be diagnosed with ASD than their Black or Hispanic peers (e.g., Kogan et al., 2009; Travers, Tincani, & Krezmien, 2011) and children from non-White minority groups were less likely than White children to have a diagnosis of ASD in their records (Mandell et al., 2009). Despite these findings, only one study to date has explored potential differences in early symptom presentation among minority and non–minority toddlers with ASD (Tek & Landa, 2012).

Objectives: This investigation of the FIRST WORDS® Project studied a sample of 364 toddlers between the ages of 18 and 36 months with ($n$ = 195) and without ($n$ = 169) a diagnosis of ASD from three racial/ethnic categories: non-Hispanic White ($n$ = 226), non-Hispanic Black ($n$ = 74), and Hispanic White ($n$ = 64).

Methods: Differences across the groups were examined using scores from an observational measure of social communication, the Communication and Symbolic Behavior Scales (CSBS; Wetherby & Prizant, 2002) Behavior Sample, and a parent-report measure of autism red flags, the Early Screening for Autism and Communication Disorders (ESAC; Wetherby, Woods, & Lord, 2007). The seven cluster scores of the CSBS Behavior Sample include emotion and eye gaze, communication, gestures, sounds, words, understanding, and object use. The ESAC provides a total score based on 30 items.

Results: After controlling for maternal education, findings revealed differences between children with and without ASD for both the CSBS and the ESAC. Non-Hispanic White toddlers were observed to score higher than non-Hispanic Black and Hispanic White toddlers on the understanding cluster of the CSBS, but racial/ethnic groups did not differ on the other six clusters. There were no significant interactions between diagnostic classification and race/ethnicity on either the CSBS or the ESAC. A large, negative correlation was observed between the CSBS and the ESAC such that children with lower social communication scores based on observation during the CSBS had higher parent report of autism red flags.

Conclusions:

These findings indicate good agreement between observed social communication and parent report

of autism red flags in a diverse sample of toddlers. There were no significant differences across race/ethnicity for six of the seven clusters of the CSBS. Results from this study suggest that both measures could be instrumental in identifying young toddlers with ASD from these racial/ethnic categories and may contribute to improving early detection and access to early intervention for toddlers with ASD.

**132.006** Early Cognitive and Developmental Predictors of ASD in Infants with Tuberous Sclerosis Complex. S. S. Jeste*[1], J. Wu[2], T. Shimizu[1], V. Vogel-Farley[3], M. Sahin[4] and C. A. Nelson[4], (1)*UCLA Center for Autism Research and Treatment*, (2)*UCLA*, (3)*Children's Hospital Boston*, (4)*Boston Children's Hospital*

Background: The Tuberous Sclerosis Complex (TSC) is an autosomal dominant disorder caused by mutations in either the TSC1 or TSC2 genes, and it is characterized by the widespread growth of hamartomas in multiple organ systems, including the brain. Rates of ASD in TSC range from 25-60%, much higher than the 1-2% reported in the general population. The diagnosis of TSC is often made prenatally or in early infancy, either through the visualization of cardiac rhabdomyomas or in the setting of early onset seizures and/or infantile spasms. In this setting, TSC represents a promising high-risk group for the investigation of early developmental trajectories and risk factors for ASD.

Objectives: We have performed a longitudinal, prospective study of infants with Tuberous Sclerosis Complex (TSC), with the overarching goal of defining early clinical, behavioral and biological markers of autism spectrum disorder (ASD) in this high-risk population.

Methods: Infants with TSC and typically developing (TD) controls were recruited as early as 3 months of ages and followed longitudinally until 36 months of age. Data gathered at each time point included detailed seizure history, developmental testing using the Mullen Scales of Early Learning (MSEL), and social-communication assessments including the Autism Observation Scale of Infancy (AOSI). Several electrophysiological paradigms were also performed, with one highlighted here involving the assessment of low level visual processing using a visual evoked potential paradigm. At 18, 24 and 36 months, a diagnostic evaluation for ASD was performed using the Autism Diagnostic Observation Schedule (ADOS) and clinical assessment by a trained clinician.

Results: Infants with TSC demonstrated delays confined to non-verbal abilities, particularly in the visual domain, through the first 6 months of life, which then generalized to more global delays by age 9 months. The delay in visual reception at 6 months was associated with electrophysiological markers, namely a longer latency of the occipital P1 component (TSC mean latency 131.8 msec, TD mean latency 120.3 msec, p=0.009). 55% (22/40) of the infants with TSC followed longitudinally were diagnosed with ASD. Both 12-month cognitive ability in all domains (verbal and non-verbal) and developmental trajectories over the second two years of life significantly differentiated the groups. More specifically, byy 12 months of age, the ASD group demonstrated significantly greater cognitive delays and a significant decline in non-verbal IQ from 12-36 months.

Conclusions: This is the first prospective study of development in infants with TSC, and it represents a timely effort to define early markers of ASD in this high-risk population. The early delay in visual reception and fine motor ability in the TSC group as a whole, coupled with the decline in non-verbal ability in infants diagnosed with ASD, suggests a domain-specific pathway to ASD that can inform more targeted interventions for these infants.

**132.007** Differences Between Preschool Children with ASD Ascertained By Clinical Referral Versus Longitudinal Follow-up of Infants with an Affected Older Sibling. L. Zwaigenbaum*[1], S. E. Bryson[2], S. Georgiades[3], L. A. R. Sacrey[1], J. A. Brian[4], I. M. Smith[5], W. Roberts[6], P. Szatmari[6], C. Roncadin[7], N. Garon[8], T. Vaillancourt[9], E. Fombonne[10], P. Mirenda[11], J. Volden[1], C. Waddell[12], T. Bennett[3], M. Elsabbagh[13], E. K. Duku[3] and A. Thompson[3], (1)*University of Alberta*, (2)*Dalhousie/IWK Health Centre*, (3)*Offord Centre for Child Studies & McMaster University*, (4)*Holland Bloorview Kids Rehab/ University of Toronto*, (5)*Dalhousie University / IWK Health Centre*, (6)*University of Toronto*, (7)*Peel Children's Centre*, (8)*Mount Allison University*, (9)*University of Ottawa*, (10)*Oregon Health & Science University*, (11)*University of British Columbia*, (12)*Simon Fraser University*, (13)*McGill University*

Background: Early development in autism spectrum disorders (ASD) is increasingly studied using prospective 'high-risk' designs, focused on infants at risk of the disorder by virtue of having

an affected older sibling. However, the comparability of children with ASD ascertained from these high-risk cohorts versus those ascertained by clinical referral from the community has never been examined, which is relevant to the generalizability of findings across groups.

Objectives: To compare the sex ratio, symptom severity and adaptive functioning of preschool children with ASD ascertained from a high-risk longitudinal sibling cohort (HR-ASD) to those diagnosed following referral to a specialized assessment clinic (clin-ASD).

Methods: The HR-ASD group (n=94) were identified as part of an ongoing multi-site prospective study of HR siblings. ASD diagnoses were established shortly after the child's 3rd birthday, using the Autism Diagnostic Interview – Revised (ADI-R), Autism Diagnostic Observational Schedule (ADOS) and expert clinical judgement based on DSM-IV-TR. The clin-ASD group (n=176) were identified from an inception cohort of clinically referred children with ASD participating in a multi-site longitudinal study. To ensure comparability by age, only children diagnosed at age 3 were included. Categorical variables (sex, language level) were compared using the chi-squared ($\chi^2$) test, and continuous variables (e.g., adaptive functioning, indexed by the Vineland Adaptive Behavior Schedule – II; VABS-II) were compared using ANOVA.

Results: The clin-ASD group was slightly older than the HR-ASD group (41.2+3.9 vs 38.7+3.4 months, $F_{1,262}$=31.8, $p$<.001). Sex ratio differed between the HR-ASD (2.2:1) and clin-ASD groups (5.1:1) ($\chi^2(1)$=7.51, $p$=.006). ASD symptoms, indexed by the ADOS severity metric and ADI-R social, communication and behavioral subscales were less severe in the HR-ASD group (all $p$s<.001; effect sizes 0.54-0.86). There were marked differences in parent-reported language level (on the ADI-R), with phrase speech in 79 of 94 children (84.0%) in the HR-ASD group, compared to 63 of 166 children (38.0%) in the clin-ASD group ($\chi^2(2)$=51.5, $p$<.001). As well, the HR-ASD group had higher levels of overall adaptive functioning, as indexed by VABS-II Adaptive Behavior Composite Standard Scores (78.1+1.4 vs 71.8+10.7, $F_{1,241}$=16.1, $p$<.001). ANCOVAs incorporating sex and age (within the narrow range studied) as covariates did not detect any main or interactive effects for these variables, and HR-ASD versus clin-ASD differences remained essentially the same.

Conclusions: Compared to clinically referred children with ASD, those ascertained from a HR cohort had less severe ASD symptoms, higher levels of language and adaptive functioning, and proportionately included more girls. These differences may reflect referral and ascertainment biases across the two cohorts, with important implications for generalizability of findings from HR infant studies. As well, children (and particularly girls) with ASD with phrase speech and higher levels of adaptive functioning who are identified by surveillance of high risk cohorts may be underrepresented among clinically referred preschoolers, due to later identification in the community. Surveillance strategies must take account of heterogeneity among children with ASD in order to ensure early identification of children across the spectrum.

**132.008** A School-Based Study of Autistic Symptoms in 3-8 Year Olds in India from Parent and Teacher Report. B. Chakrabarti*[1], A. Rudra[1], M. Belmonte[2], P. Soni[3], S. Banerjee[3], S. Mukerji[3], N. Singhal[4], J. R. Ram[5] and M. Barua[4], (1)*University of Reading*, (2)*Nottingham Trent University*, (3)*Creating Connections*, (4)*Action For Autism*, (5)*Apollo Gleneagles Hospital*

Background: Despite housing ~18% of the world's population, India does not yet have an estimate of prevalence of autism and autistic traits in the general population. One reason for this lacuna has been the lack of availability of translated and validated screening and diagnostic tools for autism, which we have addressed in our previous work (Chakrabarti et al., IMFAR 2011). Estimates drawn from studies in UK and USA suggest that India could have more than 2 million people with ASC, however this prevalence estimate has never been directly verified. There is hence a critical need to measure the prevalence of autism and the distribution of autistic traits in a general population sample in India.

Objectives: To measure autistic symptoms in a school-going sample (ages 3-8) drawn from the general population in Kolkata.

Methods: Schools from all socio-economic sectors (government, private and special schools) were selected from 3 boroughs in Kolkata. Teachers filled in the Social Communication Disorder Checklist (SCDC), a 10-item initial screening

measure for autism (Skuse et al., 1995), in English or Hindi or Bengali. Parents/caregivers also filled in the SCDC, followed by the Social Communication Questionnaire (SCQ) – a 40-item diagnostic tool (Rutter et al., 1999) – and the Autism Quotient – child version (AQ-C), a 50-item tool quantifying the distribution of autistic traits (Auyeung et al., 2009).

Results:

SCDC: Teacher reports were obtained for 12764 children. 3.6% met the cut-off score of 9. Splitting the data by language shows a similar picture, with, 3.8% meeting cutoff on English, 5.49% on Hindi and 1.29% on Bengali versions of the tool. Parent response rate for SCDC was 50.1%. Interestingly, a much greater percentage met cut-off on SCDC parent report with 20.19% meeting cut off overall. Specifically, 21.67% met cutoff on English, 10.24% on Hindi, and 20.11 % on Bengali versions of the tool. Positive correlation between parent and teacher ratings were modest, but highly significant ($r=0.103$, $p<0.001$).

SCQ: Out of 2887 respondents 8.9% met the cut-off score of 15, overall. Specifically 9.64% met cutoff on English, 8.26% on Hindi, and 10.09% on Bengali versions of the tool.

AQ-C: Out of 2901 respondents 9.86% met the cut-off score of 76. Specifically, 9.48% met cutoff on English, 11.25% on Hindi and 8.67% on Bengali versions of the tool.

Conclusions: This study provides preliminary data on the distribution of autistic symptoms in 12764 children in India, and is the first and largest study of its kind in India so far. The estimates reported suggest considerable over-reporting by parents in comparison to teachers, irrespective of language. This provides important directions for future epidemiological research into autism in India.

## 133 Molecular and Cellular Biology

*Organizer:* E. DiCicco-Bloom *Robert Wood Johnson Medical School*

**133.001** Persistent Cortical Angiogenesis and Neuronal Migration in the Young Autism Brain. E. C. Azmitia*[1], M. Alzoobaee[1], H. J. Chen[1], G. Jiang[1], V. Lee[1], A. S. Saini[1] and P. Whitaker-Azmitia[2], (1)*New York University*, (2)*State University of New York, Stony Brook*

Background: We propose a prolonged period of angiogenesis and neurodevelopment in our collection of postmortem brains from autistic donors (2.8-20.8 years of age). In autism, the brain shows accelerated postnatal growth (Redcay and Courchesne, 2005), and neurons are smaller (Jacot-Descombes et al, 2012; van Kooten et al, 2008; Fatemi et al, 2002) and more numerous (Casanova et al, 2004). Serotonin stimulates the release of a neurite extension factor from astrocytes (Whitaker-Azmitia and Azmitia, 1994; Eriksen et al, 2002; Deng et al, 2007) and increases postnatal brain growth (Akbari et al, 1994). Serotonin fibers reach the developing cortex while neurons and glial cells migrate to form cortical layers (Foote and Morrison, 1984; Wallace and Lauder, 1983). Serotonin promotes angiogenesis in rats (Warner-Schmidt and Duman, 2008) and humans (Boldrini et al, 2012). We reported increased serotonin staining of axons in the cortex of autism donors (Azmitia et al, 2011).

Objectives: We aim to detect alterations in proliferation and migration of blood vessels, astrocytes and neurons using nestin and vimentin antibodies in cortices of autistic subjects. Other antibodies examined include a-SMA (mature pericytes, immature neurons), CD146 (immature pericytes), UEA1 (endothelial cells), GFAP (mature astrocytes) and iba-1 (microglia).

Methods: Brain tissue samples were obtained from the NYS Brain Bank for Developmental Disabilities and Aging (Staten Island, New York), the Autism Tissue Program (Princeton, New Jersey), and the NICHD Brain and Tissue Bank for Developmental Disorders (University of Maryland, Baltimore). The brains were hemisected and one hemisphere was fixed in 10% formalin. The tissue was embedded in polyethylene glycol and cut into 50 mm-thick serial sections. The sections were stored in 70% ethanol. Details of our immunocytochemical method are published (Azmitia et al, 2011).

Results: In autism brains, nestin heavily labeled precapillaries and capillary vessels in all layers of superior temporal cortex at all ages analyzed (2.8-20.8 years, n=9). In control brains, nestin labeled vessels only at the youngest ages (1.8-2.1 years, n=2), while older donors (8.6-25.6 years, n=9) showed no nestin staining. Other vascular antibodies tested showed no significant differences between autism and control

individuals. UEA1 stained endothelial cells in all cortical vessels; CD146 stained small pericytes in precapillary arterioles; and a-SMA stained immature neurons and pericytes in arterioles and capillaries. GFAP and iba-1 positive cells were frequently in close proximity to blood vessels and more reactive in autism than in control brains.

Vimentin antibodies react with filaments in immature astrocytes, neurons and pericytes. The immunostained pericytes in arterioles and capillaries were abundant in control and autism cortices. Immature astrocytes, especially in layers I-III, were more numerous in autism compared to control. Vimentin positive migrating neurons were seen in autism cortices at all ages examined, heaviest in layers IV and VI, but only seen in young control cortices.

Conclusions: Our results indicate sustained angiogenesis and neuronal migration in autism that may impact cortical size and function, integrity of the blood brain barrier and microglial infiltration. The potential involvement of extended angiogenesis may open up a new avenue for understanding and treating autism.

**133.002** Characterizing the Molecular Mechanisms Underlying Autism Using iPSC-Based Models of Neurodevelopment. D. M. Dykxhoorn*[1], B. A. DeRosa[1], H. N. Cukier[2], J. M. Van Baaren[1], M. L. Cucarro[3], J. M. Vance[1] and M. A. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*University of Miami*, (3)*Hussman Institute for Human Genomics*

Background: Although studies using animal models or autopsy samples have increased our understanding of ASD pathophysiology, many questions still remain. A major constraint in ASD research has been the paucity of disease-relevant human tissues and cells with which to study the molecular mechanisms of ASD. Since ASD is a neurodevelopmental disorder, approaches are needed that facilitate characterization of neurons during development.

Objectives: We have used patient-specific induced pluripotent stem cells (iPSCs) to begin to dissect the molecular mechanisms underlying ASD during neuronal development. IPSCs permit the analysis of neuronal cells as they differentiate from pluripotent stem cells into functionally mature inhibitory and excitatory cortical-like neurons. The development of these neurons is essential to establishing proper circuitry in many regions of the brain, particularly those that have been identified as abnormal in ASD. Using our established ASD-specific iPSC lines, we are investigating several key neurobiological mechanisms that govern GABAergic and glutamatergic synapse formation at multiple time points during *in vitro* neurogenesis.

Methods: iPSC lines were developed from peripheral blood mononuclear cells (PBMCs) isolated from individuals with autism and healthy control individuals. These iPSC lines were validated for their pluripotency and self-renewal characteristics through RNA profile analysis and ICC. Once validated, the ASD-specific and control iPSC lines were differentiated into GABAergic or glutamatergic neurons through the serial treatment with cytokines and morphogens designed to induce neurogenesis mimicking *in vivo* neurodevelopment. To reduce potential heterogeneity, specific neuronal cell types (eg. GABAergic neurons) were isolated and analyzed to identify key molecular mechanisms and functions that are altered in ASD.

Results: These ASD-specific iPSC lines are able to differentiate into neural stem cells and progenitors that give rise to electrophysiologically active cortical-like GABAergic and glutamatergic neurons. One key challenge working with stem cell derived neuronal cultures has been the heterogeneity associated with the differentiation process. This can often mask subtle changes in key cell types that may have significant effects on the disease mechanism. To reduce this inherent heterogeneity, we have developed fluorescent reporter constructs that permit the identification and isolation of specific neuronal cell types from the mixed culture. We have been able to achieve over 95% purity of GABAergic neurons by flow cytometry that can be re-plated and are viable for at least two weeks post FACS. These sorted neurons had a significantly different gene expression profile than the original unsorted neuronal culture providing a more accurate picture of the transcriptional make-up of the ASD-specific neurons. Furthermore, neurons derived from the ASD-specific iPSCs exhibit changes in transcriptional profiles compared to iPSC-derived neurons from unaffected individuals, including changes in key genes involved in synaptic functionality such as *RELN*, *NLGN3* and *NLGN4X*.

Conclusions: iPSCs provide a valuable resource for understanding the molecular mechanisms that govern ASDs and facilitate analysis of the impact that specific genetic variations have on neuronal development and functionality. The identification of disease-associated mechanisms will open up new avenues for the discovery of novel therapeutic strategies, as well as, the identification of biomarkers to improve diagnosis and early intervention.

**133.003** Epigenetic Dysregulation of SHANK3 in Brain Tissues from Individuals with Autism Spectrum Disorders. Y. H. Jiang*, L. Zhu, X. Wang, P. Wang, X. Cao, A. J. Towers, J. L. Goldstein, R. Bowman and Y. J. Li, *Duke University School of Medicine*

Background:

Although a genetic component is strongly implicated in the etiology of autism spectrum disorders (ASD), the molecular basis remains poorly understood in the majority of cases; single gene mutations and chromosomal microdeletions or duplications are found only in about 10-20% of idiopathic ASD cases. The increasing prevalence of ASD also points to the role of gene and environment interaction in ASD susceptibility. Through analysis of the Angelman and Prader-Willi syndrome imprinting region in brain tissue from individuals with ASD, we proposed a mixed genetic and epigenetic model for the etiology of ASD. A similar model has also been reported by others. Evidence from recent genetic studies suggests that dysfunction of brain synapses underlies the pathogenesis of ASD which led us to hypothesize that epigenetic dysregulation of synaptic genes may be implicated in the molecular basis of ASD.

Objectives:

To test a hypothesis that ASD have an epigenetic cause by performing DNA methylation profiling of 5 CpG islands (CGI-1 to CGI-5) in the SHANK3 gene in post mortem brain tissues from 54 ASD patients and 43 controls.

Methods:

We used bisulfite genomic sequencing and pyrosequencing methods to determine the level of DNA methylation of SHANK3 CGIs in post mortem brain tissues from individuals with ASD and controls. We also performed expression analysis in brain tissues and treated the cultured cells with DNA inhibitor and promotor

Results:

We found significantly increased overall DNA methylation (epimutation) in three intragenic CGIs (CGI-2, CGI-3, and CGI-4). The increased methylation was clustered in the CGI-2 and CGI-4 in ~15% of ASD brain tissues. SHANK3 has an extensive array of mRNA splice variants resulting from combinations of 5 intragenic promoters and alternative splicing of coding exons. Altered expression and alternative splicing of SHANK3 isoforms were observed in brain tissues with increased methylation of SHANK3 CGIs in ASD brain tissues. A DNA methylation inhibitor modified the methylation of CGIs and altered the isoform-specific expression of SHANK3 in cultured cells.

Conclusions:

This study is the first to find altered methylation patterns in SHANK3 in ASD brain samples. Our finding provides evidence to support an alternative approach to investigating the molecular basis of ASD. The ability to alter the epigenetic modification and expression of SHANK3 by environmental factors suggests that SHANK3 may be a valuable biomarker for dissecting the role of gene and environment interaction in the etiology of ASD.

**133.004** Further Evidence That Non-Coding RNAs Contribute to ASD Risk. D. B. Campbell*, G. Y. Kim and N. Grepo, *University of Southern California*

Background: We recently reported (Kerin et al, 2012, *Sci Transl Med*) that the non-coding RNA *MSNP1AS* (moesin pseudogene 1 anti-sense) is a functional element revealed by genome-wide significant association of the chromosome 5p14.1 marker rs4307059 with ASD risk (Wang et al, 2009, *Nature*). *MSNP1AS* expression was increased 12-fold in postmortem temporal cortex of individuals with ASD and increased *MSNP1AS* expression was correlated with the ASD-associated rs4307059 T/T genotype. These data indicated that the non-coding RNA *MSNP1AS*, rather than the flanking protein-coding genes *CDH9* and *CDH10*, was the functional element implicated by the chromosome 5p14.1 ASD genome-wide significant association

signal. Shortly after the first ASD GWAS report was published, another ASD GWAS report (Anney et al, 2010, *Hum Mol Gen*) indicated genome-wide significant association of the chromosome 20p12.1 marker rs4141463.

Objectives: To determine the functional element revealed by the genome-wide significant association of the chromosome 20p12.1 marker rs4141463 with ASD risk.

Methods: Bioinformatics approaches were used to determine transcripts in the chromosomal region of the ASD-associated rs4141463 marker. Northern blot was used to confirm expression and transcript orientation in the human neuronal cell line SK-N-SH. Quantitative PCR (qPCR) was used to determine the expression levels of the identified RNA transcripts in a panel of human tissues as well as postmortem temporal cortex of individuals with ASD and matched controls.

Results: Although the rs4141463 marker lies within an intron of the protein-coding *MACROD2* (MACRO domain containing 2) gene, expression of *MACROD2* is neither altered in postmortem temporal cortex of individuals with ASD nor correlated with rs4141463 genotype. Our bioinformatics approaches revealed a transcript just 10 kb from rs4141463. Northern blot and qPCR confirmed expression of the 294-nucleotide non-coding RNA *RPS10P2AS* (ribosomal protein S10 pseudogene 2 anti-sense) in the human neuronal cell line SK-N-SH. In a panel of 15 human tissues, qPCR revealed that *RPS10P2AS* was expressed at higher levels than *MACROD2* in fetal temporal cortex, adult cerebellum, and adult peripheral blood. In postmortem temporal cortex, expression of *RPS10P2AS* was increased 5-fold in individuals with ASD (P=0.002) and increased 7-fold in individuals with the ASD-associated rs4141463 C/C genotype (P=0.001). *RPS10P2AS* has high homology, in the reverse complement, to a large number of candidate target transcripts. Ongoing experiments seek to determine the transcriptome-wide impact of *RPS10P2AS* over-expression on neuronal gene expression.

Conclusions: These data indicate that multiple genome-wide significant associations with ASD implicate long non-coding RNAs. More specifically, the chromosome 5p14.1 and chromosome 20p12.1 GWAS hits both implicate long non-coding RNAs that are anti-sense transcripts of pseudogenes. Subsequent reports of attempts to replicate the original genetic finding did not provide additional support for an association of rs4141463 with ASD risk. However, the original genome-wide significant association of rs4141463 with ASD led to identification of a non-coding RNA with significantly altered expression in postmortem ASD temporal cortex. Because long non-coding RNAs are more abundant in human brain than protein-coding RNAs (Kapranov et al, 2010, *BMC Biol*), this class of molecules is likely to contribute to ASD risk.

**133.005** Serum Microrna Profiling in Children with Autism. M. M. Vasu*[1], A. Ayyappan[1], I. Thanseem[1], K. Suzuki[1], M. Tsujii[2], T. Sugiyama[1] and N. Mori[1], (1)*Hamamatsu University School of Medicine*, (2)*Chukyo University*

Background: MicroRNAs (miRNAs) are small single-stranded noncoding RNA molecules that are important for brain development and neuronal differentiation. Accumulating evidence suggests usefulness of circulating miRNAs as non-invasive biomarkers for detecting and monitoring various pathophysiological conditions related to neurodevelopment. However, no such microRNA biomarkers in blood samples have yet to be determined for autism.

Objectives: We assessed the differential expression of neurologically relevant circulating miRNAs in the serum from individuals with autism.

Methods: Total RNA, including miRNA, was extracted from the serum samples of 55 autistic individuals and 55 age- and gender- matched control subjects, and the mature miRNAs were selectively converted into cDNA. Initially, the expression of 125 mature miRNAs was compared between pooled control and autism samples. The differential expression of 14 miRNAs was further validated by SYBR Green quantitative PCR of individual samples. Receiver-operating characteristic analysis was used to evaluate the sensitivity and specificity of miRNAs. The target genes and pathways of miRNAs were predicted using DIANA mirPath.

Results: Thirteen miRNAs were differentially expressed in autistic individuals compared to the controls. miR-151a-3p, miR-181b-5p, miR-320a, miR-328, miR-433, miR-489, miR-572, and miR-

663a were downregulated, while miR-101-3p, miR-106b-5p, miR-130a-3p, miR-195-5p, and miR-19b-3p were upregulated. Five miRNAs showed a good predictive power to distinguish between control and autism. The target genes of these miRNAs were enriched in several crucial neurological pathways.

Conclusions: To the best of our knowledge, this is the first study of circulating miRNAs in autism. We have identified a set of serum miRNAs that could be used as non-invasive biomarkers for autism.

**133.006** Preclinical Autism Consortium for Therapeutics: Developing a Platform for Medications Discovery. J. N. Crawley*[1], J. L. Silverman[1], R. Paylor[2], S. Lammers[3], S. C. Dhamne[3], A. Rotenberg[3], M. Sahin[3], D. G. Smith[4] and R. H. Ring[4], (1)*University of California Davis School of Medicine*, (2)*Baylor College of Medicine*, (3)*Boston Children's Hospital*, (4)*Autism Speaks*

Background: Recent discoveries that mutations associated with autism spectrum disorder occur in genes that mediate the formation and functioning of synapses raised the possibility that effective interventions could target real-time synaptic events. We sought to develop a rigorous strategy for evaluating therapeutic targets based on synaptic mechanisms, by assembling a standardized set of assays with maximum relevance to the diversity of symptoms of autism, applied to multiple mouse and rat models of autism.

Objectives: The overarching goal of our Autism Speaks PACT initiative is to improve the early phases of medicines discovery and development for treating autism spectrum disorder. *In vivo* approaches were sought to validate mechanistic targets, speed the discovery of viable new medications, and increase the success rate of clinical trials for the diagnostic symptoms of autism. *Specific objectives*: (1) Identify mouse and rat lines with mutations in the same gene to provide cross-species corroboration; (2) Design assays relevant to the diagnostic and associated symptoms of autism spectrum disorder for relatively high-throughput analysis of symptom reversals by pharmacological treatments; (3) Replicate studies within and across sites to maximize the robustness and reliability of findings.

Methods: (a) We first considered the full range of available mouse and rat models of autism with mutations in the same gene. The two-species approach became feasible through the newly available knockout rats generated by Sage Research Labs with support from Autism Speaks. (b) We next considered which well-validated rodent behavioral assays maximize face validity to the diagnostic and associated symptoms of autism. (c) We then considered the strength of biochemical, neuroanatomical, and physiological biomarkers in the literature, to identify rodent biological assays with maximal construct validity and feasibility. External academic and industry colleagues contributed advice.

Results: (a) Based on published phenotypes of all mouse mutant models in which rat mutant models are also available, the initial four models we selected are *Cntnap2, Shank3, Pten* and *Fmr1*. (b) Behavioral assays selected include social approach, reciprocal social interactions with associated ultrasonic vocalizations, exploration of social olfactory cues, spontaneous motor stereotypies, repetitive behaviors, water T-maze reversal, open field exploration, elevated plus-maze, light/dark transitions, acoustic startle and prepulse inhibition, hot plate, novel object recognition, and contextual and cued fear conditioning. Protocols and order of behavioral tests follow the same fixed sequence in both mice and rats, and are conducted across developmental ages. (c) Global physiological analyses were selected as feasible, relevant *in vivo* biomarkers, including EEG epileptiform and gamma oscillations, and telemetry for sleep patterns and circadian rhythms. Preliminary behavioral and physiological data will be presented for the *Cntnap2* model.

Conclusions: The PACT initiative has defined a strong set of standardized behavioral and physiological assays to evaluate potential new medicines targeting synaptic pathophysiology associated with mutations in risk genes for autism. Internal replications within each species, and corroborations across two species, have been designed to provide an unprecedented level of reliability. Our platform will be made available to industrial partners to advance novel medicines with the aim of expanding and improving the pipeline from preclinical evaluation of synaptic targets to clinical trials.

**133.007** Prenatal Maternal Immune Activation Causes Postnatal Epigenetic Differences in the Adolescent Mouse Brain. B.

Paul[1], Q. Li[1], E. L. Dempster[2], C. Wong[3], P. C. Sham[1], J. Mill[4] and G. M. McAlonan*[5], (1)*The University of Hong Kong*, (2)*Institute of Psychiatry, King's College London*, (3)*MRC SGDP Centre, Institute of Psychiatry, King's College London*, (4)*Exeter University*, (5)*Institute of Psychiatry, King's College London*

Background: Epigenetic changes such as DNA cytosine methylation modulate gene function across brain and are implicated in the pathophysiology of neurodevelopmental disorders such as autism. Epigenetic changes can be caused by environmental exposures such as inflammation, and may at least partly explain why prenatal exposure to inflammation increases the risk of neurodevelopmental disorders. Our group and others have shown that mice exposed to maternal inflammation prenatally have structural abnormalities in the brain and behaviour abnormalities which are analogous to those found in autism and related conditions such as schizophrenia. The current study tested the hypothesis that prenatal inflammation alters DNA methylation in key brain regions linked to autism. These were, the striatum, linked to flexibility and repetitive behaviours in autism; and the hypothalamus, an endocrine regulatory centre which synthesizes key hormones linked to autism, namely oxytocin and vasopressin. We also carried out a pilot investigation of the methylation state of the Mecp2 gene as it has widespread gene regulatory function and, in addition to its established role in the pervasive developmental condition Rett's syndrome, its polymorphism has been linked to autism.

Objectives: To examine the epigenetic changes in the adolescent brain associated with prenatal inflammation.

Methods: We harvested brain tissue from 6 week old offspring of mice exposed to the viral analogue PolyI:C or saline on gestation day 9. We used EpiTYPER assay (Sequenom) to quantitatively analyze differences in CpG methylation of Long Interspersed Elements-1 (LINE1 or L1) as a proxy of global methylation. We also quantified CpG methylation of Mecp2 promoter region using the same method.

Results: Prenatal exposure to PolyI:C did not alter global DNA methylation in striatum but caused significant hypomethylation in the hypothalamus compared to saline controls ($t = 2.44$, $P = 0.019$). There was also significant hypomethylation of the promoter region of Methyl CpG Binding Protien2 (Mecp2) ($t = 3.32$, $P = 0.002$) in the hypothalamus in offspring exposed to PolyI:C (PolyI:C mean 26.57%, saline mean 34.63%).

Conclusions: These results provide direct experimental evidence that exposure to inflammation during prenatal life causes widespread epigenetic changes which include Mecp2 promoter methylation. They also suggest that environmental and genetic risk factors associated with neurodevelopmental disorders such as autism act upon similar pathways.

## 134 Gaze, Repetition and Social Cognition

*Organizer:* E. Pellicano *Centre for Research in Autism & Education, Institute of Education*

**134.001** Relationship Between Repetitive Behaviors and Sensory Functioning in ASD. E. L. Wodka*[1], T. Koriakin[1], N. A. Puts[2], E. M. Mahone[1], R. A. Edden[1], M. Tommerdahl[3] and S. H. Mostofsky[1], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins University*, (3)*University of North Carolina*

**Background:** Abnormal sensory functioning is among the most common behavioral concerns of parents of children with autism spectrum disorders (ASD), often causing significant family stress. Increased abnormal sensory functioning has also been linked to increased repetitive behaviors in this population using parent-report measures (e.g., Baker et al., 2008; Chen et al., 2009), with repetitive behaviors hypothesized to provide some function in self-regulation in the sensory experience. Notably, these reports have relied on parent-reported repetitive behaviors and sensory functioning. Given recently identified performance-pattern differences on measures of vibrotactile detection in ASD (Puts et al., 2013), further investigation into the relationship between performance-based measures of sensory functioning and autism symptomatology is warranted.

**Objectives:** To employ a multi-method (parent-report, performance-based) examination of the relationship between sensory functioning and repetitive behaviors in children with autism.

**Methods:** Thirty-two children with autism were identified via the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS-G). To measure sensory functioning, parent-report on the Sensory Processing Measure (SPM) and child performance

on a vibrotactile battery (e.g., Cortical Metrics-4: CM-4 detection threshold, frequency, amplitude discrimination) was completed. To measure repetitive behaviors, parent-report on the Repetitive Behavior Scale-Revised (RBS-R) and clinician observation of repetitive behaviors on the ADOS was completed. The age of the sample ranged from 8-12 years ($M$=11.0, $SD$=1.5), and participants were included with at least average intelligence (Wechsler Intelligence Scale for Children-Fourth Edition: WISC-IV Perceptual Reasoning Index: PRI: $M$=106.8, $SD$=14.9).

**Results:** Significant multi-method correlations were observed between parent-report measures (SPM Total and RBS-R Total: $r_{21}$ = .631, $p$ = .012) and between performance-based measures (ADOS Repetitive Behaviors and Single Site Amplitude Discrimination: $r_{26}$ = -.390, $p$ = .049). Notably, previous reports (Puts et al., 2013) have highlighted performance abnormalities in ASD on the Single Site Amplitude Discrimination task, where amplitude discrimination in typically developing children (TDC) decreases significantly with presentation of single site adaptation, while such effect is not observed in children with ASD. Cross-method correlations were found for only parent-reported repetitive behavior (RBS Total) and Threshold Detection Reaction Time ($r_{26}$ = -.400, $p$ = .047).

**Conclusions:** There are two key findings uncovered by this work: 1) While there is some relationship between vibrotactile response and parent-reported repetitive behaviors, no relationship between vibrotactile response and parent-reported sensory behaviors was established. 2) Children with ASD have been previously shown to perform atypically on the measure of vibrotactile response (Single Site Adaptation) that was found to be correlated with clinician-observed repetitive behaviors. Taken together, these findings provide initial support to suggest overlap between sensory functioning and repetitive behaviors in ASD, and indicate that parent-reported sensory dysfunction in ASD may be more aligned with/reflect general/global behavioral challenges, rather than the specific child sensory experience.

**134.002** Psychosexual differences between adolescents with Autism Spectrum Disorders and typically developing adolescents: results from the Teen Transition Inventory.

K. Greaves-Lord*[1], L. P. Dekker[2], K. Visser[2], A. Maras[3], A. Louwerse[3] and E. van der Vegt[2], (1)*Erasmus MC-Sophia Children's Hospital*, (2)*Erasmus MC-Sophia*, (3)*Yulius*

Background:

Information on psychosexual functioning in adolescents with autism spectrum disorder (ASD) is scarce, especially when considering self-reported information. Moreover, the assessment of psychosexual functioning is complex, since psychosexual functioning is a multi-facet concept, not only covering sexual behaviours, but also knowledge, insight, skills, desires, and cognitions.

Objectives:

This study explored differences in psychosexual functioning in adolescents with ASD and typically developing (TD) adolescents using parent and self-reported information.

Methods:

At the start of our project a comprehensive parent- & self-report assessment tool on psychosexual functioning was lacking. Therefore, a new inventory was developed, the Teen Transition Inventory (TTI). Using the TTI, we compared psychosexual functioning between adolescents with an ADI-R diagnosis of ASD (n=78) and their TD peers from the general population (n=131).

Results:

The TTI was found to be a reliable measure in assessing parent- and self-reported psychosexual functioning in adolescents with ASD and TD adolescents. Adolescents with ASD as well as their parents reported significantly less sexual knowledge, less social relational skills, less intimate experiences, more inappropriate behaviours, and a more negative self-concept than TD adolescents. No significant differences were found regarding physical development and the desire for intimacy.

Conclusions:

Since adolescents with ASD seem to have less sexual knowledge and experiences, more problematic or risky intimate behaviours and a more negative self-concept than their TD peers, future research should focus on how to promote

more optimal psychosexual functioning in adolescents with ASD.

**134.003** Associations Between Aggression and Restricted, Repetitive, and Stereotyped Behaviors and Interests in Children with Autism Spectrum Disorder: A Multi-Informant, Multi-Method Study. A. Keefer*[1], L. Kalb[2], R. A. Vasa[1], M. O. Mazurek[3], S. Kanne[3] and B. Freedman[4], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins School of Public Health*, (3)*University of Missouri*, (4)*University of Delaware Center for Disabilities Studies*

Background: Aggression in children with autism spectrum disorder (ASD) is highly prevalent and seriously impairing to the child, family, and community. Despite this burden, correlates of aggression have not been identified in this population. Although preliminary data indicate a positive association between restricted, repetitive, and stereotyped behaviors and interests (RRSBI) and aggression in individuals with ASD (Kanne and Mazurek, 2011), these studies have been hampered by methodological limitations. Therefore, detailed analysis of this relationship is critical prior to the development of targeted prevention and intervention strategies.

Objectives: To examine: a) if RRSBI is positively associated with aggression across multiple assessment methods, informants, and definitions of aggression; b) what methodological factors have a greater influence on this relationship (i.e., informant, such as teacher- or parent-report, vs. method, such as semi-structured interview or questionnaire); and c) if the definition of aggression influences this association (i.e., either narrowly defined as physical aggression, such as hitting and kicking, or aggression broadly defined across multiple behaviors, including verbal aggression and affective instability).

Methods: The sample consisted of 2648 children from the Simons Simplex Collection, a 12-site North American, university-based research study that gathers phenotypic data from families with a single child with ASD (Mean Age = 9y, SD=3.7y; 87% male; 74% Caucasian). Diagnosis was confirmed using the ADI-R (Rutter, Le Couteur, & Lord, 2003) and the ADOS (Lord, DiValorne, & Risi, 2002). Aggression was measured using two items from the ADI-R (#81, #82) and the CBCL - Aggressive Behavior Syndrome Scale (parent and teacher versions) (Achenbach and Rescorla, 2001). RRSBI was measured utilizing the Restricted, Repetitive, and Stereotyped Patterns of Behavior subscale of the ADI-R, the total score from the RBS-R (parent report) (Lam and Aman, 2007), and the Autistic Mannerisms subscale from the SRS (parent and teacher report) (Constantino et al., 2003). Multiple linear regression models were employed to calculate mean differences in RRSBI across levels of aggression while adjusting for IQ, race, household income, child gender, and maternal education. Estimates from those models were used to calculate effect sizes (Cohen's *d*) which were averaged, adjusted (for informant vs. method confounding/overlap), and compared across informant, method, and type of aggression.

Results: A significant, positive association was found for 31 of the 40 RRSBI x Aggression analyses ($p < .05$). Although the overall average effect size was small ($\Delta = .36$), there was tremendous heterogeneity in these estimates ($\Delta$ ranged from 0 to 1.19). Differences in effect sizes for informant ($\Delta = .51$) was twice as great as method ($\Delta = .25$). A similar finding was evident when aggression was broadly ($\Delta = .56$) vs. narrowly defined ($\Delta = .31$).

Conclusions: As theory suggests RRSBI to be an antecedent of aggression (Reese et al., 2003), results from this analysis suggest that interventions targeting the reduction of RRSBI may result in a concomitant reduction in aggression. Methodologically, these findings indicate differences in informant, method, and definition of aggression introduce unexplained variance into this association and should be addressed in prospective intervention studies.

**134.004** ERP Signatures of Rule Violation and Association with Repetitive Behavior in ASD. D. Bjornn*[1], A. Dohm[1], M. South[1], M. J. Crowley[2] and M. J. Larson[1], (1)*Brigham Young University*, (2)*Yale University*

Background: Although "insistence on sameness" was described as a fundamental feature of autism in Leo Kanner's original description, research into the underlying mechanisms of rigid behavior has been relatively scant. Understanding how this rigidity develops may inform targets for etiological research and for treatment. In the current study, we used event related potentials (ERP) to explore the neural time course of rule violation in ASD.

Objectives: To investigate ERP signatures in response to rule violation in ASD children and controls. Based on previous research in healthy adults we hypothesized differences in the P300

wave (associated with decision making) and a frontal slow wave from around 500-700ms.

Methods: We used the CyberShape rule violation task developed by Michael Crowley as an analog to the CyberBall social exclusion task. The participant and two virtual partners are supposed to throw to another player indicated by a target shape that matches the shape in the player's glove. But in alternating blocks of trials, one of the virtual players consistently throws to the "wrong" player.

Thirty four children 11-17 years of age, including 17 diagnosed with ASD and 17 age- and IQ-matched healthy controls, participated in the CyberShape task while being monitored using EGI's Geodesic128 channel EEG nets and Netstation software. A parent of each participant completed questionnaires regarding dimensional measures of autism symptoms (the Social Responsiveness Scale) and anxiety (the Spence Children's Anxiety Scale).

Results: No significant difference was found between groups for reaction times. ERPs were analyzed across three conditions: trials in a congruent block where there was no rule violation; trials in an incongruent block where one virtual partner threw against the rules to the other virtual player; and an incongruent condition where one virtual partner threw incorrectly to the participant. A repeated measures ANOVA using a 2 (diagnostic group) x 3 (condition) design wave found a significant main effect (highest activity for incorrect throws to the participant and lowest activity for the congruent trials) but the interaction with group was not significant. Nonetheless, for the ASD group only there was a significant negative correlation ($r$ = -.61) between mean P300 activity and the Mannerisms subscale of the SRS, suggesting that greater repetitive and restricted behavior is associated with decreased P300 response.

A frontal negativity between 300-400ms (faster than we had hypothesized) did not show an overall significant main effect but the group x condition interaction was significant. Visual inspection of the data shows that a clear main effect in the control group was obscured by a lack of differential response to condition.

Conclusions: Our results indicate that the CyberShapes task can reliably elicit neural signatures related to decision making and monitoring, and there is evidence these are related to everyday symptoms of rigid repetitive behavior in ASD. Limited ability to differentiate among different conditions of rule violation or congruence may indicate arise due to inability to extinguish response from the incongruent trials and suggest confusion induced by rule changes in the environment.

**134.005** Atypical Neural Responses to Direct Gaze from a Live Person in Autism. L. A. Harrison*[1], J. M. Tyszka[1], J. Elison[2] and R. Adolphs[1], (1)*California Institute of Technology*, (2)*University of Minnesota*

Background:

In 1943, Leo Kanner observed children with autism having "a far better relationship with pictures of people than with people themselves." While a large literature documents abnormal processing of faces and eye gaze in people with autism spectrum disorder, the vast majority of stimuli used in those studies have a series shortcomings: they are pictures or videos, rather than people in the flesh. Yet, as Kanner's quoted observation and our own experience argue, pictures and real people are processed in quite different ways, and can be dissociatively impaired in autism.

As autism is partially characterized by a persistent deficit in social interaction, it is reasonable to presume deficits, including in gaze, may be accentuated in actual interaction with another person. Findings from eye tracking studies indicate gaze behavior is influenced by the direct presence of another person. It is unknown whether direct live gaze is differently represented in the brains of individuals with autism.

Objectives:

This study comprised two main objectives. The first objective was to determine whether controls and individuals with autism are sensitive to the difference between live and recorded gaze, namely, whether the neural response to gaze changes as a function of the presence of another person. The second objective of the study was to characterize the differential neural response to live and recorded gaze in autism relative to controls.

Methods:

We explored these aims using a blocked design fMRI experiment. Participants included 15 males with autism, and 15 age, gender, and IQ-matched controls. In a Live condition, participants monitored the gaze of a live actor sitting behind the bore of the magnet. Audio instructions delivered to the actor's headphones cued their gaze: actor conditions consisted of direct gaze, averted gaze, or eyes closed. In the Recorded condition, equivalent video recordings of the Live condition were used.

Results:

Networks of activation revealed a set of partially distinct networks activated in autism compared to controls by direct live gaze. The autism and control groups were primarily differentiated by an anterior/posterior separation in the Live but not Recorded condition. Individuals with autism had less anterior, but more posterior activation during the Live condition than controls. Meanwhile, in the Recorded condition, anterior activity in autism was more similar to that of controls.

Conclusions:

We demonstrate that the neural response to live gaze is distinct in autism; an interactive experiment was necessary to capture this difference. This finding provides significant insight into the difficulty individuals with autism face in interacting with other people in everyday life.

**134.006** Modeling Dynamic Mental Representations of Facial Expressions of Emotion in Autism Spectrum Disorders. K. Ainsworth*[1], O. Garrod[1], R. E. Jack[2], J. Lee[3], R. Adolphs[3], P. Schyns[1] and D. R. Simmons[2], (1)*The University of Glasgow*, (2)*University of Glasgow*, (3)*California Institute of Technology*

Background:

Autism Spectrum Disorders (ASDs) are characterized by a deficit in understanding others' emotions [Hobson, 1986a, JCPP, 27,321-342]. However, there is debate about whether individuals with ASD are impaired in the perception of facial expressions of emotion [Harms, 2010, Npsych Rev,20,290-322]. We addressed this issue using a unique, 4D Generative Face Grammar [GFG; Yu, et al., 2012, Comput. Graph., 36,152–162] which combines state-of-the-art computer graphics technology with robust psychophysical techniques (reverse correlation) to model the mental representations of facial expressions of emotion in individual observers.

Objectives:

To identify differences in mental representations of the six basic facial expressions of emotion between ASD and typically developed (TD) controls, with specific focus on facial muscle groups and their temporal dynamics.

Methods:

Stimulus generation and task procedure are similar to those used in Jack, et.al., [2012, PNAS, 109,7241-7244]. On each trial, the GFG randomly selects a set of Action Units [AUs, Ekman & Friesen, 1978, Consulting Psychologists Press] from 41 possible AUs and six temporal parameters. By combining these parameters, a random, but physiologically plausible, facial animation is produced, rather like pulling random strings on a facial puppet

(http://www.psy.gla.ac.uk/~kirstya/emotions/example_stim2.html). Ten ASD observers categorized 2400 same-race stimuli according to the 6 basic emotions (happy, surprise, fear, disgust, anger and sadness) or 'other' and rated intensity of the emotion on a 5-point scale. Sixty TD controls also performed the same task.

Results:

To model the mental representations of each facial expression of emotion, we correlated each observer's responses with the AUs, intensity and temporal parameters. We derived 60 ASD facial expression models (10 observers x 6 emotions) and compared them with 360 TD models (60 observers x 6 emotions).

*Spatial (i) – Similarity matrices*

To identify the similarities and differences of the mental representations of facial expressions between ASD and TD observers, we computed the similarity (Hamming distance) between ASD and TD models. ASD observers showed markedly different compositions for fear, anger and sadness compared to TD observers.

*Spatial (ii) – Bayesian classifiers*

Using Bayesian classifiers (split half method, 1000 iterations), we computed classification of the ASD models across time and showed higher levels of inconsistency in the categorization of anger, fear and sadness within the ASD group.

*Spatio-temporal*

We analysed spatio-temporal dynamics of AU and intensities across time using a t-test on model intensity rating differences ("emotion gradient") between ASD and TD groups. Results show that whereas TD observers are sensitive to intensity in the middle of the time course of the facial expression, ASD observers are not.

Conclusions:

So far, our analysis of dynamic mental representations of facial expressions of emotion in ASD show (1) differences in how fear, anger and sadness are represented in ASD compared to TD (2) classification accuracy is lower in fear, anger and sadness within ASD observers, indicating variance across ASD observers; (3) ASD observers are less sensitive to intensity in the middle of the facial expression time course. This new approach provides significant insights into emotion perception in ASD and also helps to explain inconsistencies found in previous studies.

**134.007** Adults with Autism Display Increased Gaze to Low-Level Visual Features When Viewing Dynamic Social Videos. D. P. Kennedy*[1], N. Gandhi[2] and R. Adolphs[3], (1)*Indiana University*, (2)*University of California, San Diego*, (3)*California Institute of Technology*

**Background:** Abnormalities in social attention emerge early in individuals with autism spectrum disorders (ASD), and represent a core aspect of the phenotype across the lifespan. The vast majority of experiments that have examined social attention in ASD have used highly constrained tasks and stimuli in order to attempt to isolate specific cognitive and attentional abnormalities. These types of experiments, though essential and have provided important insight into attentional abnormalities, result in artificial scenarios that often fail to capture some of the key characteristics of social stimuli as they exist in the real world (e.g., dynamic, multi-modal, complex, subtle, continuous, etc.). An alternative approach, and the one used here, is to use stimuli that better approximates that which would be encountered in the real world.

**Objectives:** To determine the factors underlying gaze abnormalities in ASD when viewing dynamic social scenes.

**Methods:** We recorded eye movements from 20 adult ASD participants and 34 neurotypical control participants at 300Hz while they watched and listened to a full episode of the television show The Office ("Pilot"; © NBC Universal; 22 minutes in length, divided into 3 clips). This stimulus was chosen for several reasons, which included long moments uninterrupted by camera cuts, multiple actors on the screen at once, often subtle emotional expressions, and socially awkward interactions (social *faux pas*). Participants were instructed simply to watch the video and pay attention. Initial analyses described below were carried out on data from the first clip. We only included data from a participant if there was less than 2° of error across the entire screen both before and after the video was shown. Similarity across individuals was quantified using the Normalized Scanpath Saliency method along with a leave-one-out-approach.

**Results:** We found that ASD and control groups differed overall in how they viewed the video. The gaze pattern in controls was more similar to other controls, and less similar to those with autism ($p < 0.001$), while the gaze pattern in individuals with ASD was less similar to controls and more similar to others with ASD, suggesting a common pattern of abnormal gaze in ASD. Group differences in gaze persisted regardless of the number of people in the frame (0, 1, 2, or 3 people) (all $p < 0.05$), suggesting perhaps non-social factors might account for group differences. Using a well-described computational model of visual saliency (Itti-Koch), we found that when gaze diverged between groups, individuals with ASD were more likely to fixate pixels with higher intensity (i.e., brightness). This finding was replicated using data from the second clip.

**Conclusions:** These findings replicate prior results that individuals with ASD display abnormal attention to social stimuli, but we further demonstrate that abnormal patterns are common across individuals with ASD, with a bias toward looking at high-intensity areas of the scene. Studies aimed at further elucidating the mechanisms underlying social (and non-social) attentional differences in ASD will be essential to understand how they might give rise to aspects of the autistic phenotype, and for developing novel targets of intervention.

**134.008** Visual Exploration As a Measure of Social Motivation in ASD.
K. Gotham*[1], K. E. Unruh[2], N. J. Sasson[3], L. Turner-Brown[4], G. S. Dichter[5] and J. W. Bodfish[6], (1)*Vanderbilt University*, (2)*Vanderbilt Brain Institue*, (3)*University of Texas at Dallas*, (4)*University of North Carolina at Chapel Hill*, (5)*Duke University*, (6)*Vanderbilt University School of Medicine*

**Background:** We should use precision when discussing social impairment, a cornerstone symptom domain of ASD. Currently, social affect generally is measured in terms of coarse global ratings based on distinct behaviors and summary impressions. Latent to this aggregate measurement, we hypothesize that there are independent though related dimensions, such as social -cognition, -interest, and -anxiety, that may interact across development to create various profiles of social ability or impairment. To evaluate the utility of isolating these social dimensions, we must establish psychometric or psychophysiological methods of measuring them.

**Objectives:** To explore a visual exploration eye-tracking (ET) task as a potential measure of social interest by comparing ET data across ASD and typically developing (TYP) cohorts, and assessing its association with psychometric measures of social anxiety, social cognition, and experienced pleasure in social and nonsocial events.

**Methods:** Our sample included participants with high functioning ASD (HFA; n=71), as well as gender-, age-, and IQ-matched TYP (n=64) controls (*HFA*: $M_{age}$=12.2 years, $SD_{age}$=3.0 years; $M_{IQ}$=101.7, $SD_{IQ}$=17.4; *TYP*: $M_{age}$=12.7 years, $SD_{age}$=3.0 years; $M_{IQ}$=112.2, $SD_{IQ}$=14.9). The protocol included a passive viewing ET paradigm that probes visual salience (Sasson et al., 2008). This "Visual Exploration Task" consists of complex arrays that contain social (e.g., pictures of people) and nonsocial stimuli (e.g., pictures of objects). Fixation and exploration patterns were compared across the diagnostic groups and also were assessed for association with several socially-relevant psychometric measures, including subscales of the Social Responsiveness Scale (SRS; Constantino et al., 2003), Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000), Multidimensional Anxiety Scale for Children (MASC; March, 1997), Anxiety Depression and Mood Scale (ADAMS; Esbensen et al., 2003), and ratings of anticipatory and consummatory pleasure in social and nonsocial events respectively (Temporal Experience of Pleasure Scale; TEPS, Gard et al., 2006).

**Results:** In preliminary analyses of the first 44 HFA and 30 TYP with coded ET data, the ASD group showed reduced exploration (number of images fixated) of social images (HFA $M$=14.0(4.6), TYP $M$=19.2(5.0), $p$<.05) coupled with increased duration of fixation on nonsocial images (HFA $M$=479 ms (227), TYP $M$=423 ms (174), $p$<.05). Composite severity of social deficits was modestly positively correlated with exploration of nonsocial images within the ASD group ($r$=0.37, $p$=.04). HFA demonstrated significantly greater deficits than TYP on the SRS Social Motivation, ADAMS Social Avoidance, MASC Social Anxiety, TEPS Anticipatory and Consummatory subscales ($F$'s[1,73] ranging from 17.3-156.1; all $p$'s<.001). ET data on the rest of the sample has been collected and is currently being processed, such that within- and across-group associations linking ET and psychometric data will be presented for the entire sample.

**Conclusions:** Valid measures of social interest in ASD (i.e., those minimally confounded by social anxiety and the social skill deficits that mark this population) will allow us to explore variability of social interest in ASD by subgroups and across development. This also may inform the development of individualized treatment: for some individuals, building social motivation and/or targeting social anxiety may boost effects of targeted interventions on social cognition.

## 135 Randomized Intervention Trials: Replications, Novel Methods and New Applications

*Organizer:* L. R. Watson *University of North Carolina at Chapel Hill*

**135.001** Double-Blind, Placebo-Controlled Trial of D Cycloserine Given Prior to Peer Mediated Social Skills Training in Youth with an Autism Spectrum Disorder: Initial Findings. L. K. Wink*[1], N. Minshawi-Patterson[2], R. Shaffer[3], S. Hurwitz[4], M. Plawecki[2], C. J. McDougle[5] and C. Erickson[1], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Indiana University School of Medicine*, (3)*Cincinnati Children's Hospital Medical Center*, (4)*Indiana University, Bloomington*, (5)*Massachusettes General Hospital*

Background: No drugs are FDA approved for use targeting the core social impairment of autism and related pervasive developmental disorders (PDDs). Glutamatergic dysregulation is implicated in the pathophysiology of PDDs, now termed ASD. D-Cycloserine (DCS) is FDA approved for the treatment of tuberculosis and the drug is known to impact NMDA glutamate receptor neurotransmission. DCS has been shown to potentiate learning when given prior to therapy sessions in the anxiety disorder literature.

Objectives: We evaluated the efficacy of DCS given 30 minutes prior to peer mediated social skills training (SST) in youth aged 5 to 11 years with ASD.

Methods: We conducted a double-blind, placebo-controlled trial of low dose (50mg) DCS given prior to manualized SST in 68 children aged 5 to 11 years with ASD over 10 weekly sessions. SST sessions each included 4 youth with ASD and 2 age-matched typically developing peers trainers along with two clinician group facilitators. In addition to evaluating primary and secondary outcome measures after 10 weeks of SST, we additionally conducted a follow up evaluation for each participants 3 months following the SST. Participants with ASD were required to have a full scale IQ greater than 70, meet DSM IV-TR criteria for autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specified (PDD-NOS) based upon clinical interview and results from the Autism Diagnostic Interview Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS). Our primary outcome measure was the total score on the Social Responsiveness Scale (SRS). Key secondary outcome measures included the Clinical Global Impresisons Improvement (CGI-I) and Severity (CGI-S) scales, the Aberrant Behavior Checklist (ABC), Pediatric Quality of Life Inventory, 4th Edition, and the Vineland-II. We additionally compiled structure observational behavioral data coding with each session to track potential change with treatment throughout the SST.

Results: Sixty-eight youth were enrolled in this trial. The results will be available in Spring 2014. Top line results reviewing the primary and key secondary outcome measures will be reported for the drug versus placebo groups in May 2014.

Conclusions: Preliminary conclusions will be generated following the dissemination of top line results in May 2014.

**135.002** Early Social Interaction Project for Toddlers with Autism Spectrum Disorder: Identifying Active Ingredients of Treatment. A. M. Wetherby*[1], V. P. Reinhardt[1], C. Schatschneider[2], W. Guthrie[1], R. D. Holland[1], J. Woods[1], L. Morgan[1] and C. Lord[3], (1)*Florida State University Autism Institute*, (2)*Florida Center for Reading Research*, (3)*Weill Cornell Medical College*

Background: The priority of early detection of autism spectrum disorder (ASD) has led to the need for developmentally appropriate yet evidence-based intervention. The Early Social Interaction Project (ESI) is a parent-implemented intervention for toddlers with ASD that teaches parents to embed transactional supports and strategies in everyday activities to achieve the intensity needed for toddlers with ASD in a cost-effective way. A randomized controlled trial of ESI compared two 9-month conditions of varying intensity: 1) parent-implemented intervention (PII) offered in 3 individual weekly sessions for 6 months and then 2 weekly sessions for 3 months to teach parents how to embed supports in everyday activities to support the child's active engagement 25 hours a week; and 2) an information, education and support group (IES)

offered weekly for 9 months. Previous analyses (Wetherby et al., 2013) documented significant improvements on child outcome measures of social communication and language after 9 months in treatment, with children in PII demonstrating more significant gains on social communication (CSBS Communication; Vineland Socialization), language skills (Mullen Receptive Language, Vineland Communication), and adaptive behavior (Vineland Daily Living Skills) than children in IES.

Objectives: The aims of this study were: 1) to examine how changes in parents' use of transactional supports mediate observed differences between children in PII and IES after 9 months in treatment; and 2) to examine the growth trajectories of parent's use of transactional supports over 9 months of treatment.

Methods: Participating families (*n*= 82) were video-recorded during monthly home observations to measure the parent engaging the child in interaction during everyday activties for an hour. Home observations at baseline, 3, 6, and 9 months of intervention were coded for parents' use of 8 transactional supports using the *Measure of Active Engagement and Transactional Support*(MAETS; Wetherby, Morgan, & Holland, 2013).

Results: Aim 1: Mediation analyses were used to examine whether the amount of transactional supports used by parents would explain the differential growth in communication, language, and adaptive behavior by the PII and IES groups. Using bootstrapping to conduct mediation analyses, results indicate that the amount of transactional supports parents used mediated all observed treatment effects at 9 months. Aim 2: Results indicate that while parents in both PII and IES showed significant growth in their use of transactional supports, parents in PII showed faster growth, using more transactional supports earlier. Growth curves of each support were compared by intervention group and follow-up regions of significance analyses were used to estimate the time point at which the PII and IES groups diverged in their use of supports. Parents in PII surpassed those in IES in their use of transactional supports by 90 days in intervention.

Conclusions: Analyses indicated that the measure of transactional supports fully mediated the child intervention outcomes, highlighting the promising role that parents play in intervention delivery of for toddlers with ASD. These findings suggest that features of PII may be critical to support parent's acquisition and use of transactional supports within the first three months of treatment.

**135.003** Randomized Multisite Replication of Early Start Denver Model Outcomes. S. J. Rogers*[1], A. M. Estes[2], C. Lord[3], N. Lange[4], J. Munson[2] and G. Dawson[5], (1)*UC Davis M.I.N.D. Institute*, (2)*University of Washington*, (3)*Weill Cornell Medical College*, (4)*McLean Hospital*, (5)*Duke University*

Background**:** Dawson et al (2010,2012) reported widespread improvements in outcomes of young children with ASD treated for two years for 15 hours per week with Early Start Denver Model, a manualized, comprehensive individualized intervention fusing developmental and behavior analytic methods. The ESDM group significantly surpassed a randomized comparison group in IQ gain, language, adaptive behavior, autism symptoms and diagnostic changes. Furthermore, an EEG study revealed normalized patterns in the ESDM group involving stronger responses to social than nonsocial stimuli, a pattern opposite that of the comparison group.

Objectives: The objectives of this study were to replicate the original ESDM study in a large, randomized, multisite, controlled trial.

Methods**:** 98 children with ASD, without medical risk factors, between 15 and 28 months of age, were randomized into either 20 hours per week of ESDM for 24 months or to community treatment at three sites. There were no significant differences in participant characteristics across sites, and no significant differences between experimental and comparison participants on any dimension. ESDM intervention was delivered in homes by paraprofessionals trained and supervised by professional staff and averaged 14.8 hours per week. Treatment fidelity measures demonstrated that all sites delivered the intervention at acceptable, and similar, levels. All measures were gathered pretreatment, after 12 months of treatment, and after 24 months of treatment.

Results: Significant differences in outcomes across sites required that we analyze each site separately, rather than pooling of data. Two of the three sites replicated the ESDM advantage in

IQ and language previously reported. In site 1, in which the comparison group averaged more intervention hours than did the ESDM group, the ESDM group mean IQ significantly increased from 69 to 90 while the comparison group increased from 67 to 85. In site 2, mean IQ increased from 73 to 91 compared to the comparison group from 68 to 67. In contrast, in site 3, the comparison group made greater IQ gains (from 67 to 83) than did the ESDM group (64 to 72), though the increases in both groups were significant. There were significant drops in autism symptom severity in both assignment groups in all sites. Significant group differences in language occurred in 2 sites.

Conclusions: This randomized multisite study demonstrated significant developmental improvements related to ESDM assignment in two of three sites, with the mean IQ gains in those sites mirroring or surpassing the IQ gain reported in the original study. It is interesting that in this study and in many others, treatment effects are much larger for developmental variables rather than for core autism symptoms. Developmental variables, rather than autism severity per se, are the best predictors of outcomes and therefore these improvements are critical for later functioning. Significant effects of ESDM compared to randomized comparison groups have now been demonstrated at three, independent sites. This demonstrates that, according to Nathan and Gorman's criteria, ESDM is an efficacious, empirically validated 1:1 intervention model for young children with ASD.

**135.004** Mindfulness Based Stress Reduction (MBSR) and Cognitive Behavioral Therapy (CBT) for Adults with Autism Spectrum Disorder (ASD) - Preliminary Results. B. B. Sizoo*, *Dimence*

Background: The prevalence of ASD among the adult population is estimated to be 1 percent. Despite high rates of anxiety and depression among adults with ASD, treatment methods for these comorbid conditions have not been systematically studied or compared in this patient population. Recently, Mindfulness Based Stress Reduction (MBSR) and Cognitive Behavioral Treatment (CBT) protocols were adapted for adults with ASD and could be excellent candidate therapies for reducing anxiety and depression.

Objectives: To study the ability of both treatment methods to reduce anxiety and depression symptoms among adults with ASD, and to determine which therapy is best suited for which patient.

Methods: A three-arm RCT among 90 adults with ASD (30 MBSR, 30 CBT, and 30 treatment as usual, (TAU)), was conducted in an outpatient setting with measurements at the start and end of the 14 week treatment period, and at 3 months follow-up. Prior informed consent and medical ethical approval was obtained. Instruments included the hospital anxiety and depressions scale, rumination, irrational belief and mindfulness scales, and an autism symptom checklist.

Results: Preliminary results indicate that both MBSR and CBT lead to a significant reduction in anxiety and depression among adults with ASD. Both MBSR and CBT were superior to TAU. There was no gender or age effect. Effectiveness in relation to patient characteristics will be discussed.

Conclusions: Mindfulness and cognitive behavioral therapies are promising treatment methods to reduce comorbid anxiety and depression in adults with ASD.

**135.005** Braingame Brian: A Randomized Controlled Trial for an Executive Functioning Training for Children with ASD. M. de Vries*[1], P. J. Prins[1], B. A. Schmand[2] and H. M. Geurts[1], (1)*University of Amsterdam*, (2)*Academic Medical Center Amsterdam*

**Background:** There is an urgent need for effective interventions for children with autism spectrum disorders (ASDs). Current interventions focus mainly on teaching social or communicative skills, and appear to be relatively unsuccessful. Few studies focused directly on fundamental abilities such as executive functioning (EF). Children with ASD are known to experience difficulties in EF. Hence, training EFs seems promising, especially since EF interventions show positive effects in disorders highly comorbid with ASD such as ADHD.

**Objectives:** Two EF interventions - a working memory (WM) training, and a cognitive flexibility training - are studied in a large randomized controlled trial of children with ASD. The objective is to improve the trained EF (near transfer), and to obtain generalization of improvement to other EFs (far transfer), and to EFs in daily life (far transfer).

**Methods:** Children with ASD (n=102, 8-12 years, IQ>80) are randomly assigned to one of three interventions; a WM-, cognitive flexibility-, or non-EF training (active control condition) build into a computer game (Braingame Brian). The training consists of 25 sessions (40 minutes each), performed within six weeks. Each session contains both WM and cognitive flexibility training tasks. The task to be trained (e.g., WM in the WM training) increases in difficulty adaptive to performance, whereas the other task remains at a low level. To examine efficacy of the training, WM (Corsi), cognitive flexibility (switch task), and everyday EF (BRIEF) are measured pre-training, post-training, and 6-week-follow-up.

**Results:** Currently, data of 76 children are complete. In January 2014, data of all children will be complete. Preliminary analyses reveal that 1) Corsi performance of all children improved during the training, and remained stable at follow up. More importantly, children who received WM training improved more than children who received flexibility training, and marginally more than children who received non-EF training. 2) On the switch task all children decreased in error switch costs (difference between errors on switch and repeat trials), but increased in reaction time (RT) switch cost (difference between RT on switch and repeat trials) after the training, but overall RT decreased. Surprisingly, this improvement was manifested between post-training and follow-up. Switch task performance did not differ between the interventions. 3) All children improved on the WM, flexibility and total scale of the BRIEF, but there were no differences between the interventions. The dropout rate was 25%.

**Conclusions:** The WM training seems to induce near transfer; children who received WM training improved most in WM. However, the WM training does not seem to induce far transfer, i.e. both cognitive flexibility and daily life EF did not improve more than in children who received flexibility or non-EF training. The flexibility training induced neither near, nor far transfer. Children who received flexibility training did not improve more in flexibility, WM, or daily life EF compared to children who received WM or non-EF training. Since there are large individual differences within ASD, we will also apply multilevel techniques in the final analyses to find possible predictors of training outcome and compliance.

**135.006** Here's Looking at You: Neural Effects of a Cognitive-Behavioral Social Skills Treatment on Eye Gaze Processing in Children with Autism—a Randomized, Comparative Study. K. Ibrahim*[1], L. V. Soorya[2], D. B. Halpern[3], S. Soffes[3], M. Gorenstein[3], P. M. Weinger[3], J. D. Buxbaum[3] and A. T. Wang[3], (1)*University of Hartford*, (2)*Rush University Medical Center*, (3)*Icahn School of Medicine at Mount Sinai*

Background: Social deficits are a hallmark of ASDs and may be related to underactivity in key brain regions involved in social cognition. There is also evidence that activity in normative neural networks can be increased significantly by providing children with ASD with explicit instructions to attend to important social cues. Social skills training using a cognitive-behavioral (CBT) approach has been shown to be effective in improving social behavior deficits in children with ASDs. However, there is a need for a greater understanding of the neural mechanisms underlying the behavioral changes in response to treatment. Further work is also needed to provide more randomized controlled trials with larger sample sizes and comparative treatment groups.

Objectives: This study examines the neural effects of a 12-week social skills treatment on the neural correlates of processing gaze in faces depicting varying emotions. A CBT approach was compared with a child-directed play approach.

Methods: Verbally fluent children with ASD, 8-11 years of age, were randomized to the CBT or child-directed comparison group. Both treatments consisted of 12 weekly 90-minute sessions (4-6 children in each group with a 1:2 therapist to child ratio) with a concurrent parent component. The CBT treatment addressed 3 skill areas: Nonverbal communication, Emotion recognition, and Theory of mind Training (NETT). Behavioral assessments and fMRI were conducted at baseline, end of treatment, and at a 3-month follow up. While undergoing fMRI, children viewed images of emotionally expressive faces depicting anger, fear, disgust or a neutral expression. Faces displayed either a direct or averted gaze looking to the observer's right or left. Regression analyses were conducted to evaluate the relationship between brain activity and changes in social cognition and behavior.

Results: Following treatment, children in the CBT group showed greater activity in the medial prefrontal cortex (MPFC), the ventrolateral PFC, temporoparietal junction (TPJ), and the superior

temporal gyrus (STG) relative to baseline. These changes were most pronounced for the averted gaze condition. In contrast, children in the comparison group did not show any regions of increased activity post- vs. pre-treatment. When directly comparing the two groups on changes in brain activity, we found that children in the CBT group showed greater increases in regions relevant for theory of mind (MPFC and TPJ) and emotion recognition (STG) relative to the comparison group.

Conclusions: Findings from this study suggest that there may be an advantage to using a group cognitive-behavioral approach in increasing activity in social brain networks. Specifically, capitalizing on top-down explicit processing while reinforcing attention to key social cues, such as gaze direction, from the bottom up may facilitate perspective taking and thus lead to increased activity in the social brain network. Further analyses are being conducted as it will be important to assess whether these changes are maintained at follow up. This study contributes to our understanding of the neural underpinnings of the social deficits in autism and the plasticity of networks involved in social cognition underlying response to treatment.

**135.007** Is Parent Child Interaction Therapy Efficacious for Families with Young Children with Autism Spectrum Disorder?. N. C. Ginn*[1], L. Clionsky[2], C. Warner-Metzger[3], J. P. Abner[4] and S. Eyberg[5], (1)*University of North Carolina*, (2)*Baylor College of Medicine*, (3)*University of Chicago Medical Center*, (4)*Milligan College*, (5)*University of Florida*

Background:

The Child Directed Interaction (CDI) phase of Parent Child Interaction Therapy (PCIT) emphasizes following the child's lead in play and increasing parent-child attachment (Harwood & Eyberg, 2006) and may be a particularly promising intervention for children with autism spectrum disorder (ASD). CDI has been associated with increased prosocial behaviors and decreased parent stress across child populations including those with disruptive behavior problems (Eisenstadt, Eyberg, McNeil, Newcomb, & Funderburk, 1993), anxiety disorders (Choate, Pincus, Eyberg, & Barlow, 2005), and intellectual disability (Bagner & Eyberg, 2007). CDI also shares similarities with naturalistic teaching interventions because it focuses on a child-led play situation which creates an environment in which the child views play, as well as parent-child interaction, as a positive, rewarding experience and promotes social and communicative learning as well as skill generalization (Masse, McNeil, Wagner, & Chorney, 2008). Together, the shared features of parent based and naturalistic interventions as well as research support for behavioral change following CDI in other populations suggests that CDI may be an effective intervention for families with a young child with ASD.

Objectives:

The purpose of the study was to examine the efficacy of the CDI phase of PCIT in a randomized control trial with young children with ASDs for improving child social and behavioral functioning as well as changing parenting behaviors and stress.

Methods:

Participants were 30 families with children ages 3 to 7 with a previous diagnosis of ASD. Families were randomized into either the Immediate treatment (IT) or the Waitlist (WL) condition. Treatment consisted of a total of 8, weekly sessions of manualized CDI, in which families received live coaching of the treatment skills during play with their child. To assess parenting behaviors, families participated in a child-led play situation which was coded using the Dyadic Parent–Child Interaction Coding System (DPICS) to examine parenting behaviors. Parents also completed the Parent Stress Index, Social Responsiveness Scale, and the Eyberg Child Behavior Inventory at pre-, post-, and 6-week follow up assessments.

Results:

Parents in the IT condition reported significantly fewer child disruptive behaviors, $F(1,27)= 16.56$, $p < .001$ $d = 1.12$, as well as gains on the Social Awareness subscale, $F(1,27)= 6.82$, $p = .02$, $d = 1.03$ when compared to the WL condition. Across 8 sessions mothers learned to provide positive attention to their children's appropriate social and play behaviors, $F(1, 27) = 92.45$ , $p < .001$, $d = 2.60$. No differences in total parenting stress were found, however, parent distress associated with disruptive behavior was reduced $F(1, 27)= 6.73$, $p$

= .02, *d*= 0.79. All outcomes were maintained at 6-week follow up.

Conclusions:

Following CDI, children showed less disruptive behaviors and more awareness of social cues; and parents demonstrated improved positive parenting skills and reduced distress associated with child externalizing behaviors. This study has important implications as it suggests that a relatively brief, time-limited intervention that is widely accessible to families can lead to clinically significant and meaningful changes for families with a child with ASD.

**135.008** Feasibility and Efficacy of Virtual Reality Job Interview Training in Adults with Autism Spectrum Disorder. M. J. Smith*[1], E. J. Ginger[1], M. A. Wright[1], K. Wright[1], J. L. Taylor[2], L. B. Humm[3], D. E. Olsen[3], M. D. Bell[4] and M. Fleming[1], (1)*Northwestern University Feinberg School of Medicine*, (2)*Vanderbilt Kennedy Center*, (3)*SIMmersion LLC*, (4)*Yale University*

Background: The community-based unemployment rate for adults with an autism spectrum disorder (ASD) ranges from 50-75%. Moreover, evidence-based services to support these adults in finding employment are sparse. The job interview is a common gateway to obtaining competitive community-based employment, but it can be a significant barrier for individuals with ASD to obtain employment. Improving job interview performance is a critical target for employment services and is especially important for individuals with ASD given their significant social deficits.

Objectives: To test the feasibility and efficacy of the internet-based 'Virtual Reality Job Interview Training' (VR-JIT) program

Methods: VR-JIT consists of up to 10 hours of simulated job interviews with a virtual human resource representative and didactic job interview education materials. In a randomized single-blind controlled trial, 26 adults with autism aged 18-31 years were randomized to VR-JIT (n=16) or to a treatment as usual (TAU) control condition (n=10). The primary outcome measures were improved performance on standardized job interview role-plays and a measure of job interview self-confidence. Within the VR-JIT condition, change in trial performance over time was examined as a process measure.

Results: Regarding feasibility, participants attended 90% of VR-JIT training sessions and reported that the training was easy-to-use, helpful, and enjoyable. They also reported that training increased their confidence and prepared them for future interviews. Regarding efficacy, participants in the VR-JIT condition had greater improvement in standardized role-plays than TAU participants (p=.046). A similar pattern was observed with regards to self-confidence at the trend level (p=.060). We also found a log linear increase in the training scores for the simulated job interview trials over time (R-Squared=.83).

Conclusions: The current study was a novel attempt to demonstrate changes in vocational skills through virtual reality training using an internet-based platform that can be widely used by families, support groups, and service providers. The findings provide preliminary evidence that VR-JIT is both feasible and efficacious for adults with ASD.

## 136 Innovative Technology Demonstration

These poster presentations highlight an area of technology and its application to autism spectrum disorder.

**136.201 201** A Characterization Study of Q&a Behavior on an Online Forum for Autism. H. Hong*, G. D. Abowd and R. Arriaga, *Georgia Institute of Technology*

### A Characterization Study of Q&A Behavior on an Online Forum for Autism

**Background:** Recent work has demonstrates the potential of using social media to help young adults with autism increase their independence by providing socially-acquired advice about their daily needs. While much is known about the general area of challenges faced by individuals with autism, little is known about what they are really concerned with on a daily basis and how they address such concerns in the form of question-asking or requests for help through social media.

**Objectives:** The goal of this study was to understand how individuals with autism seek advice on everyday life challenges through the use of an online forum, AspiesCentral (AC). We wanted to determine how well this forum served as a social Q&A system for these individuals, and how it might be improved. By considering what questions they ask, and how those questions are asked and answered, we seek design insight to improve the online experience. Specifically, we

want to determine whether and how to improve the quality and the timeliness of answers to the kinds of everyday questions that individuals with autism have.

**Methods:** we present a study of an online forum, AspiesCentral (AC), for adults that self-identify as being on the autism spectrum. Using a dataset of 28,960 posts organized into 1,945 threads, this paper explores in depth question-asking behaviors of individual users. Drawing on a combination of quantitative analysis and qualitative observations, we examine the posts we collected to better understand the pattern of question-asking behavior. Finally, we explore how the quality of responses to questions posed on the forum (i.e., rate and time) is affected by other properties of the question, such as the target responders and the perceived urgency of the response explicitly and implicitly indicated in a question.

**Results:** We found that AC was used to receive advice and answers on a variety of topics. AC users asked question differently compared to what is known in other general population social Q&A systems. First, they tended to reveal more personal details in their questions. Second, they asked questions to simply confirm that others feel as they do or that others empathize with the issues raised. Despite the effectiveness of AC as a social Q&A system, it did demonstrate drawbacks: 1) unless specifically requested, responses for urgent matters were not addressed in a timely fashion; and 2) some topics requiring particular interests or expertise could not be sufficiently covered by existing AC members.

**Conclusions:** These drawbacks represent real design opportunities to either improve online forums like AC or to create other social networking solutions. Scaffolding of questions through a smart template or natural language critiquing system can prompt responders for quicker answers to urgent matters. This scaffolding can also better support questions that make clearer the intended form of response. In addition, mechanisms or incentives need to be in place that will encourage qualified crowdworkers from the general population to provide answers that represent more diverse and needed areas of expertise.

**136.202 202** A Computerised Approach to Interviewing for ASD: Evidence for 3di's Value in Translation, and International Compatibility with DSM-5 Criteria.

R. H. Warrington*[1], H. Berntsen[2], J. Chuthapisith[3], W. De La Marche[4], K. Lai[5], M. C. Lai[6], W. Mandy[1], S. Merelli[7], F. Mo[5], K. Puura[8], A. Rattazzi[9], D. H. Skuse[1] and G. Slappendel[10], (1)*UCL Institute of Child Health*, (2)*Akershus University*, (3)*Ramathibodi Hospital, Mahidol University*, (4)*University of Leuven*, (5)*Chinese University of Hong Kong*, (6)*National Taiwan University College of Medicine*, (7)*San Paolo Hospital Medical School*, (8)*Tampere University and University Hospital*, (9)*PANAACEA*, (10)*Erasmus MC - Sophia Kinderziekenhuis*

**Background:**

The Developmental, Dimensional and Diagnostic Interview (3di) is a computerised diagnostic parental interview, designed for deep phenotyping of the autism spectrum. Technically, the 3di offers patented advantages to facilitate the interviewing process. All variables (individual questions and summary scales) can be downloaded for statistical analysis. In line with revisions to the definition of ASD in *DSM-5,* the 3di question set and associated algorithms (formerly emulating ADI-algorithms and DSM-IV.TR) have recently been modified. There is considerable current interest in providing methodologies that will permit reliable recording of the ASD phenotype across languages and cultures; in May 2013 the WHO resolution *Comprehensive and Coordinated Efforts for the Management of Autism Spectrum Disorders*was sponsored by more than 50 countries. The computerised structure of the 3di lends itself to efficient and reliable translation, and recent research has demonstrated its utility in this regard.

**Objectives:**

The objective of the technical demonstration will be, first, to provide evidence for the value of the 3di's computerised interviewing procedure to facilitate both clinical assessments and research, based on the new DSM-5 criteria for ASD and Social Communication Disorder. The demonstration will encourage hands-on use of the interview and illustrate key features including data downloading procedures. Second, the demonstration will showcase technical innovations that facilitate translation into any language (with all text tailoring features intact), as well as the ease of exporting responses from any translation in a standard format for analysis (e.g. SPSS), thus permitting the compilation of cross-cultural

databases containing high-density phenotypic data.

**Methods:**

In order to test the effectiveness of the 3di to emulate *DSM-5* algorithms in translation, we recently derived diagnostic scores for each symptomatic subdomain, and tested them using Confirmatory Factor Analysis, in both an English and a Finnish version of the interview, on a total sample of 708 individuals with varying degrees of autistic trait severity. After testing the *DSM-5* model in our Finnish ASD data, we proceeded formally to compare its fit in both UK and Finnish samples. We ran a series of ever more constrained models simultaneously in both translations, to conduct an increasingly rigorous and in-depth test of the *DSM-5* model's factorial invariance.

**Results:**

Factor loadings and estimates of fit of the *DSM-5*model were similar in both UK and Finnish translation. This provides strong evidence for the validity of the translation process into Finnish. Previous research has shown the 3di has equivalent high sensitivity and specificity in Thai translation as in English. Currently, Cantonese, Dutch, Finnish, Mandarin, Norwegian, Spanish, and Thai translations are available. Italian and Taiwanese translations are nearing completion, Arabic, Hindi, Swahili, and French translations are pending. Training courses in countries as diverse as the Netherlands and Argentina demonstrate high degrees of inter-rater reliability can be achieved in translation, with minimal hands-on instruction.

**Conclusions:**

Computerisation of the interview process for deep phenotyping of ASD facilitates translations that have excellent construct and predictive validity based on DSM-5 diagnostic criteria. Design innovations permit excellent inter-rater reliability to be achieved rapidly with minimal training, at low cost.

**136.203 203** A Manualized Wireless Moisture Alarm Intervention for Teaching Toileting in Children with Autism. D. W. Mruzek*[1], S. A. McAleavey[2], W. A. Loring[3], E. Butter[4] and T. Smith[2], (1)*University of Rochester Medical Center*, (2)*University of Rochester*, (3)*Vanderbilt University*, (4)*Nationwide Children's Hospital*

**Background:** For many children with autism, development of toileting skills is delayed relative to the general population, resulting in increased demands on the family and decreased independence for the child. Because of this, a toilet training method that is user-friendly, relatively rapid and effective is needed. In this study, we developed a methodology that entails a novel enuresis alarm and a corresponding parent training manual and are currently comparing the effectiveness of this toilet training method with a standard intervention.

**Objectives:** Objectives of this study are: (1) to develop the technology and corresponding manualized treatment; (2) obtain preliminary data on the feasibility, acceptability, and perceived helpfulness of the enuresis alarm intervention compared to a standard behavioral intervention in children with autism.

**Methods:** The enuresis alarm (or "pager") consists of an Ipod-based app that interfaces with a transmitter and disposable moisture sensor positioned in the child's underwear that activates upon contact with small amounts of urine. The device has the following features: (1) auditory and/or vibratory page of parent and/or child at the onset of a toileting accident; (2) maintenance of a time-stamped record of accidents; (3) instant Bluetooth electronic data transmission for timely clinician review of data and feedback; (4) picture-based reinforcement menu for child; (5) "reminder" page for parent and child for prompting "dry pants checks" and independent initiation of toileting. The treatment program consists of a manualized parent-training program divided into distinct modules from introduction to fading and generalization. This experimental toilet training technology and corresponding training manual are currently being compared with a standard behavioral intervention (i.e., ATN Toilet Training Tool Kit) in a pilot randomized trial with 30 children with autism (aged 3 - 5) at three diverse sites in the US.

**Results:** Field-testing of the device indicates a high degree of durability and sensitivity to the onset of urination, as well as a minimum of false positives or negatives. Parent-training and implementation of device for toilet training progressing successfully with data suggesting effectiveness in at least some instances.

**Conclusions:** The iPod-based enuresis alarm and corresponding treatment manual may offer a viable alternative to lengthy and difficult standard behavioral intervention for parents of children with autism. Opportunity for near-immediate clinician feedback, time-stamped accident data and relative ease of training procedure may present advantages that aid families and their clinicians overcome training difficulties. Our preliminary data support conducting a larger trial to test efficacy of the alarm and manualized parent training program.

**136.204 204** A Pilot Study of the Vayu Vest: Effects of Deep Pressure Stimulation on Performance and Physiological Arousal. S. E. Reynolds*[1], S. J. Lane[1] and B. Mullen[2], (1)*Virginia Commonwealth University*, (2)*Therapeutic Systems*

Background: Use of deep pressure touch has been used in clinical practice based on the assumption that it changes physiological arousal. This assumption is grounded in a variety of literature bases, include sensory integration theory. Unfortunately evidence for use of deep pressure touch is severely lacking, and the research that does exist includes inconsistent application without any objective measures of physiological arousal.

Objectives: To test the effects of deep pressure stimulation, applied through an FDA-approved Vayu Vest, on both performance and autonomic arousal in a normative sample. We hypothesized that deep pressure input would decrease sympathetic arousal and improve measures of attention/performance.

Methods: Research was conducted in a laboratory setting at a public research university. A convenience sample of twenty two adults (mean age 23.2 yrs) participated in the study. The study design is a repeated measures, repeated baseline design in which participants complete a performance test before and after deep pressure application. Deep pressure is self-applied through the Vayu Vest which is donned by the subject and inflated using a hand pump. Performance was measured by counting the number of errors committed while playing an ipad game, the Moron Test. Autonomic data was collected using our Mindware system; seven electrodes were placed on the participants' chest and back and two on the hand. Physiological variables include skin conductance level, mean heart rate, and respiratory rate.

Results: Average performance on the first Moron Test was 7.0 errors; the average for the second test was 5.5 errors. Preliminary analysis of the skin conductance data show an average decrease from the start of the session when the vest is inflated (mean SCL 8.35) to the end of the session when the vest is deflated (mean SCL 5.05).

Conclusions: The data suggest that wearing the Vayu Vest, even for a very short period of time (3 minutes), reduces sympathetic nervous system arousal and may positively impact performance. This research work-in-progress has the potential to provide objective data supporting the use of deep pressure touch in therapies for children with autism spectrum disorders.

Demonstration: We will offer the opportunity for conference attendees to don the Vayu Vest and have electrodes applied to their hand in order to demonstrate the use utility of our portable physiology equipment (Mindware System) and the Vest itself. Participants will be able to observe real-time changes in arousal on a laptop computer before, during, and after vest-wear and while participating in a stressful ipad game.

**136.205 205** A Step Towards Anxiety-Sensitive Virtual Reality Based Social Communication Platform: Implication on Physiology for Children with Autism. S. Kuriakose*[1], P. Kumar[1], P. Raghavan[2] and U. Lahiri[1], (1)*Indian Institute of Technology, Gandhinagar*, (2)*Our Ashiana*

Background:

Social stories can be an effective way in addressing the core social communication deficits in children with autism spectrum disorder (ASD). Effective skill-learning is possible when an individual learns from his comfort zone with diminished level of anxiety. Anxiety disorders in children with ASD may be considered both as possible cause and consequences of their social communication deficit. Providing a platform that monitors the anxiety of these children may be beneficial. Specifically, children with ASD have difficulty in explicitly expressing their affective states, which places limits on conventional observational techniques. The anxiety-sensitive platform can be used to overcome such limitations using physiological markers of one's affective states. Among the available technology-assisted techniques we chose Virtual Reality (VR) for developing the social communication platform along with physiology as a tool for prediction of

one's affective state. In India, with prevalence rate of 1 in 250 children with autism, and scarce trained resources, research on technology-assisted systems for these children is necessary.

Objectives:

The presented work seeks to address the deficits in social communication of children with ASD by (i) developing a VR-based social communication task module considering language and subtle social aspects specific to Indian context, which are valuable contributors to social communication (ii) interfacing the VR-based system with physiological data acquisition module, and (iii) designing a usability study to recognize the feasibility of VR-based social communication platform to map one's physiological signals to his affective state of anxiety, thereby having implication on one's performance.

Methods:

VR-based social conversation system was designed which projected humanoid characters with real-life faces having an Indian look, as classmates of the participant. These avatars moved dynamically in context-relevant VR environment while displaying gestures and narrating social stories in regional languages to the participants during task presentation. Also they demonstrated different context-relevant emotions e.g., happy, angry and neutral. Different difficulty levels depending on the type of questions asked by the avatars following the task presentation were also a part of the system design. Simultaneously the participants' physiological signals e.g., heart rate, skin temperature, etc. were monitored via wireless wearable biosensors. A therapist rated the participants on their anxiety level. The participants' performance was assessed based on their response to questions asked by the avatars.

Results:

Two children with ASD and three typically developing (TD) children participated in a usability study. Results indicate that both ASD and TD groups showed variations in their physiological signals. These variations had implication towards their performance. For ASD group the variations were high compared to their TD counterparts. This can be attributed to their high anxiety level as rated by the therapist during the study.

Conclusions:

The work presented here, shows the feasibility of a VR-based social conversation module that can switch tasks of varying difficulty based on one's performance measure has the capability to predict participants' anxiety level from their physiological markers. The preliminary data analysis shows the potential of developing a physiology based anxiety-sensitive intelligent adaptive VR platform to address the social communication challenges faced by these children.

**136.206 206** A Video Analysis of Children with ASD Spontaneously Initiating about Discrepancies in a Virtual Environment: Interaction Profiles and General Trends. A. M. Alcorn[1], H. Pain[1], J. Good[2] and S. Fletcher-Watson*[1], (1)*University of Edinburgh*, (2)*University of Sussex*

Background:

The rigidity of thought and desire for routine which characterise ASDs might yield predictions that novel and expectation-violating aspects *(discrepancies)* within a *virtual environment* (VE) might be upsetting. An evaluation of ECHOES, a touchscreen-based, game-like VE to support social communication, provided an opportunity to investigate the effect of various types of discrepancies on children's communication. Activities deliberately introduced novelty, such as new objects and effects, but intermittent software issues meant that ECHOES also included *unintentional* surprising events, such as the virtual character making "mistakes" in an activity he had already done correctly, and non-events, like known objects being absent from activities. Observations of young children with ASD using ECHOES suggested that discrepancies can actually be successful extrinsic motivators of spontaneous and positive initiations to both human and virtual partners (Alcorn, Pain, & Good, 2013).

Objectives:

The current analysis sought to better illuminate how discrepancies might be incorporated into the design of future VEs, with the overall goal of motivating initiation. It closely examined individual children to determine which discrepancies motivated them to initiate, and what the characteristics of those initiations were;

this information builds up a picture of children's interaction style.

Methods:

Video observation (n=8 participants, developmental age 2-6) was used to locate discrepant aspects (novelty, surprising events, and non-events) during children's play with the ECHOES VE. Child reactions were recorded as non-social or as initiation to a partner (human or virtual). Initiations were subsequently tagged for their apparent function (imperative or social) and constituent behaviours. Current analysis examined each child's reactions along a series of dimensions (e.g. discrepancy type, function) to develop an *interaction profile* summarising his or her customary patterns of activity when engaging with ECHOES discrepancies (e.g. child's prevalence of non-social reactions vs. initiations, specific initiation behaviours, etc.)

Results:

While each child showed a unique profile, children could be grouped into several higher-level profiles representing general styles of interaction with the ECHOES discrepancies and social partners. Each one was characterised by a cluster of apparent "preferences" for certain types of discrepancies over others, and common manners of reaction. Profiles had no strong relation to children's developmental age. As a general trend, children with a high proportion of their total reactions regarding novelty showed a low proportion of reactions to non-events, and vice versa.

Conclusions:

Examining interaction profiles can flesh out our picture of the relatively new phenomenon of discrepancies as motivators for communication, and help to illuminate what it is that children understand about discrepancies. Work currently in progress is investigating how discrepancies may be embedded in the design of new VEs, with the goal of supporting initiations. Interaction profiles are a valuable tool throughout the process of developing VEs and other interactive technologies: at the design stage they form the basis of user personae, and in a finished system they allow the included discrepancies to be customised to particular subgroups of children, thus maximising the likelihood of their initiation.

**136.207 207** ASC-Inclusion – a Virtual Environment Teaching Children with ASC to Understand and Express Emotions.

S. Newman*[1], O. Golan[2], S. Baron-Cohen[3], S. Bolte[4], A. Baranger[5], B. Schuller[6], P. Robinson[3], A. Camurri[7], N. Meir-Goren[1], M. Skurnik[1], S. Fridenson[2], S. Tal[2], E. Eshchar[2], H. O'Reilly[8], D. Pigat[8], S. Berggren[4], D. Lundqvist[4], N. Sullings[5], I. Davies[3] and S. Piana[7], (1)*Compedia*, (2)*Bar-Ilan University*, (3)*University of Cambridge*, (4)*Karolinska Institutet*, (5)*Autism Europe*, (6)*Technische Universität München*, (7)*University of Genova*, (8)*Autism Research Centre, University of Cambridge*

Background:

Children with Autism Spectrum Conditions (ASC) experience difficulties communicating their own emotions and recognizing the emotions of others. These difficulties appear in different modalities, including facial expressions, vocal intonation, and body language. Such deficits may hamper the social functioning of children with ASC and increase their exclusion.

Alongside these difficulties, individuals with ASC tend to have intact and sometimes superior abilities to comprehend and manipulate closed, rule-based, predictable systems, such as computerized environments, and may better learn from them than from non-structured settings. Computerized environments can produce simplified versions of the socio-emotional world, reduce sensory stimulation, and support a featured-based learning style of socio-emotional cues, gradually integrating them into a holistic picture. Harnessing these qualities for the sake of emotion recognition and expression training, children with ASC may be more motivated to learn about the emotion world through virtual computerized environments.

Objectives:

To demonstrate the up to date status of the project, as well as a summary of data collected so far for its evaluation.

Methods:

The program is embedded in a virtual world and includes highly engaging elements, aimed at enhancing the child's motivation, including games, animation, video and audio clips, rewards, a child's avatar, and communication with smart agents and peers.

The system combines several state-of-the art technologies in one comprehensive environment, including computerized analysis of users'

gestures, facial and vocal expressions. It is planned to be available for home or school use, and as an aid to therapists.

Caregivers will be offered their own supportive environment, including professional information, reports of child's progress and use of the system and forums for parents and therapists. Based on the internet, it will allow families from wider and less privileged environments to benefit from professional training.

An iterative process of testing, feedback and evaluation supports the system's development. Panels of children with ASC and their families, and panels of professionals, in the UK, Israel, and Sweden, contribute to ensure content and usability will comply with the users' preferences and needs.

Results:

The current presentation will demonstrate:

1. The system at its current stage of development: its virtual world and emotion recognition training in the different modalities, as well as the expression training components, using the above technologies for analysis and feedback on the children's' performance. The environment, tutorials and games presented have been evaluated and approved by our panels of families and professionals.

2. Preliminary results of the multi-site RCT, conducted with 120 children in Israel, Sweden and the United Kingdom.

Conclusions:

The ASC-Inclusion project offers children with ASC and their families the benefit of state of the art educational technology for enhancement of their socio-emotional communication repertoire. A multi-site randomized controlled trial is in process and preliminary results are being analyzed.

**136.208 208** Attention Point: Improving Identification in Rural Communities Using an Interactive Digital Video Library. A. B. Barber*, L. G. Yerby and D. Albertson, *University of Alabama*

**Background:**

Children with ASD living in rural communities experience later diagnosis (Mandell, et al., 2005), poor accessibility to specialists (Siller et al., 2013), and limited exposure to evidence-based interventions (Stahmer, 2009). Novel, culturally sensitive techniques must be developed to improve identification in rural settings (Yudell et al., 2012) so that children and families have the same access to quality interventions as children living in urban areas. Video sharing provides a solution for improving early identification in rural communities while also increasing physician knowledge of early red flags using their own patients.

**Objectives:**

The purpose of this research is 1). To develop and implement an interactive digital video library, *Attention Point*, in rural medical health clinics; and 2). To establish the feasibility of using *Attention Point*so that rural physicians can share video of children at risk for autism with a university-based ASD Clinic and retrieve processed video clips to support early identification.

**Methods:**

The University of Alabama Autism Spectrum Disorders Clinic, Institute for Rural Health, and the School of Library and Information Studies partnered with 3 rural health clinics to implement this project. Children who failed the M-CHAT (Robins, et al., 1999) participate in 15-minute video-recorded parent-child semi-structured play samples. Video observations are securely shared with the University of Alabama Autism Clinic via *Attention Point.* Next, the project team scores the CARS-2 (Schopler et al., 2010), which is embedded into the program, and provide detailed feedback to the rural physicians. Annotated comments regarding observed social interaction, nonverbal and verbal language, and repetitive behavior are used to process and segment the videos, which in turn highlight observed red flags. Finally, the project team provides referral suggestions for early intervention, autism-specific testing, and/or other appropriate referrals to the physician. The resulting collection of notable video clips of observed red flags can be used to educate rural physicians and nurses on early signs of autism thereby improving their patient care.

**Results:**

Preliminary efforts of this project have so far included the development of a prototype video digital library, *Attention Point*, as one outcome from a resource development project, funded by the National Library of Medicine (HHS-N-276-2011-00004-C). Currently, project investigators are piloting *Attention Point* with one partnering rural health clinic. Data collection is ongoing. *Attention Point* will be demonstrated and data will be presented regarding the number of children identified with ASD using *Attention Point* in our targeted rural health practice as well as qualitative data regarding physician's experiences using *Attention Point.*

**Conclusions:**

The project uses innovative technology to give rural children with ASD access to quality specialized healthcare while also educating rural physicians on early signs of ASD in their own patients. *Attention Point*offers a promising first step to removing the disparity of diagnosis delay in our rural communities, thereby significantly enhancing a child's potential to have optimal intervention outcomes. Findings can have an immediate benefit on rural areas that experience delays in autism identification and intervention.

**136.209 209** Capturing Social Motor Coordination in Children with Autism: Comparing the Microsoft Kinect, Video Analysis and Wireless Motion Sensor Tracking. V. Romero*[1], J. L. Amaral[1], P. Fitzpatrick[2], C. L. Thomas[3], A. W. Duncan[4], H. Barnard[4], R. C. Schmidt[5] and M. J. Richardson[1], (1)*University of Cincinnati*, (2)*Assumption College*, (3)*Cincinnati Children's Hospital*, (4)*Cincinnati Children's Hospital Medical Center*, (5)*College of the Holy Cross*

Background:

Motor deficits have long been associated with autism but the role they play in social and emotional functioning is poorly understood. In addition, social movement coordination has been shown to facilitate social connection and may be abnormal in children with autism (Fitzpatrick et al., 2013). Recent advances in technology have resulted in a number of low cost gaming systems for remotely tracking human motor behavior that could potentially improve our understanding of bodily coordination exhibited by children with autism. Software development kits that enable the development of recording software that meet the specific needs of researchers interested in obtaining wireless time-series recordings of human movement has also made it much cheaper and easier to collect data. The degree to which these systems can replace expensive motion tracking systems, however, is unknown.

Objectives:

Here we present a comparison of skeletal data recorded using the Microsoft Kinect to data obtained using video analysis algorithms and a Polhemus Latus wireless motion tracking system. By comparing data recordings of various motor coordination behaviors obtained from a study on social motor coordination in typically developing children and children with autism, we detail the effectiveness of each system for studying social motor behavior in these populations.

Methods:

50 typically developing children and 50 children with autism from 72 to 131 months of age were asked to coordinate with a male experimenter in six tasks and to play pat-a-cake. The movements of the participants and the experimenter were recorded using a Kinect and a Polhemus system. From the Kinect we obtained both skeletal movement data and video. The time-series data obtained were then compared using dynamical time-series analysis.

Results:

All three data capturing methods revealed differences in the coordination that occurred for both groups. Children with autism exhibited less movement coordination with the experimenter overall. The magnitude of this difference, however, was task by method dependent. The most robust data collection method was the Polhemus system, which was able to capture differences in the fine grain patterning of motor coordination. The video analysis method provided the best measure of fully body coordination. The Microsoft Kinect skeletal data provided an adequate measure of global and, in some cases, local coordination, but overall was less robust than the other two.

Conclusions:

All sources proved useful in capturing motor coordination data. The type of task and experimental set-up, however, played a significant role in the success of each. The Polhemus system provided the most robust fine grain time-series data, but was limited to tasks that employed sensored limbs. Both the video analysis and the Kinect skeletal data provided better measures of global coordination, but were both strongly affected by occlusion. In order to obtain measures of movement for two separate individuals using video analysis or Kinect skeletal data participants' movements must not overlap. To obtain useful Kinect skeletal data the participants must also face the recording systems more or less directly. Measuring motor coordination using these techniques may provide a better window into the underlying coordination problems in autism.

**136.210 210** Care Alert: A Technology to Prevent Elopement. M. Rowe*, *University of South Florida*

Background: Children with ASD are at increased risk for missing incidents in which the child leaves a safe situation and goes missing in the community. Over half of these incidents begin from the home setting. In these incidents a child who is left temporarily unsupervised either intentionally or unintentionally slips away unnoticed and doesn't return. Often the parent observed the child only minuter prior to the incident. Unfortunately some of these children won't be found before dying, usually due to drowning but also in vehicular accidents. The stress of continuous vigilance is draining for parents and unrealistic in a home setting. Currently no technologies are designed specifically to monitor a child within a home and provide immediate and direct notification to the care provider of the child's movements through the home, near exit doors, and through exit doors. Products are particularly needed to assist parents in monitoring the child during the night while parents are sleeping.

Objectives: The purpose of developing CareAlert was to provide an in-home monitoring system that could be used to monitor an individual with cogntive impairment. Additionally the purpose of this project was to utilize scientific methods to test the acceptability and effectiveness of the system.

Methods: Product development was funded with Small Business Technology Transfer (STTR) awards from the National Institute of Nursing Research. Subsequently a small business was formed to bring this product to market.

Results: CareAlert has the following characteristics: monitors without the child wearing any devices; alarms at the site of the caregiver, not at the location of the child; easy to install and use; multiple integrated safety features to facilitate nightly activation, variable alarms depending on the severity of the situation; mobile control panel that can be used throughout the home; and self-monitoring of system health. The system has been fully tested in persons with dementia and use resulted in an 85% reduction in nighttime events. A pilot study has been conducted in homes of child with ASD. In the pilot, there was strong acceptability and easy usability of the system by the parents. Children tolerated the system well. In the 6 families in which full 6-month data were available, there were trends toward reductions in parent nighttime awakenings which were accompanied by decreases in stress scores and better sleep quality. A full trial of the effect of CareAlert in improving child and parent sleep as well as reducing the consequence of fragmented sleep is in the planning stages.

Conclusions: CareAlert represents a novel and tested technology designed particularly to prevent home elopements in persons with cognitive impairment. This technology may be particularly useful in homes of children with ASD. The technology is market ready with units being produced from the initial manufacturing tooling. A demonstration of CareAlert will be provided.

**136.211 211** Children-Robot Interaction: Eye Gaze Analysis of Children with Autism during Social Interactions. S. Mavadati*[1], H. Feng[1], S. Silver[1], A. Gutierrez[2] and M. H. Mahoor[1], (1)*University of Denver*, (2)*Florida International University*

**Background:**

Children with *Autism Spectrum Disorder (ASD)*demonstrate a deviant pattern of mutual eye gaze that is visible in early ages and may lead to other social deficits (e.g. delaying development of social cognition and affective construal processes). Currently, clinical work employing intensive behavioral and educational programs to teach individuals with ASDs appropriate social skills in an effort to make them more successful in

social situations. However, an empirical question remains regarding the effectiveness of these training approaches to teach the fundamental face-to-face communication skills, such as understanding and regulating facial expressions and visual attentions in the social environment. Recent studies reveal that children with ASD have superior engagement to the robot-based interaction, and it can effectively trigger positive behaviors (e.g. eye gaze attention). This suggests that interacting with robots may be a promising intervention approach for children with ASD.

**Objectives:**

The main objective of this multidisciplinary research is to utilize humanoid robot technology along with psychological and engineering sciences to better improve the social skills of children with *High Functioning Autism (HFA)*. The designed intervention protocol focuses on different skillsets, such as eye gaze attention, joint attention, facial expression recognition and imitation. The current study is designed to evaluate the eye gaze patterns of children with ASD during verbal communication with a humanoid robot.

**Methods:**

Participants in this study are 14 male children ages 7-17 (M=11 years) diagnosed with ASD. The study employs NAO, an autonomous, programmable humanoid robot to interact with ASD children in a series of conversations and interactive games across 3 sessions. During different game segments, NAO and children exchange stories and having conversation on different context. During every session of the game, five cameras recorded the entire interaction of a child and NAO. Videos were later scored to analyze the gaze patterns of the children for two different contexts. Studying eye gaze fixation and eye gaze shifting while: 1) NAO is speaking; 2) child is speaking.

**Results:**

To analyze the eye gaze of participants, every frame of video was manually coded as *Gaze Averted*('0') or *Gaze At*('1') w.r.t NAO. To accurately analysis the gaze patterns of children during the conversation, the video segments of 'NAO speaking' and 'child speaking' have been selected. The averages of four measures were employed to report the static and dynamic properties of eye gaze patterns:

1) 'NAO speaking': Gaze At NAO *(GAN)*= %55.3, Gaze Shifting *(GS)*=%3.4, GAN/GS = 34.10, Entropy GS: 0.20

2) 'child speaking': *GAN* = %43.8, *GS*=%4.2, GAN/GS = 11.6, Entropy GS = 0.27

Where '*Entropy GS*' refers to uncertainty of eye gaze shifting and is within a range of [0-1].

**Conclusions:**

The results indicates that children with ASD having more eye contact and less gaze shifting while NAO is speaking (Higher GAN/GS and lower Entropy GS), however they prefer to shift their gaze more often and have less fixation on the robot as they are speaking. These results will serve as an important basis to significantly advance the emerging field of robot-assisted therapy for children with ASD.

**136.212 212** Computational Vocal Arousal: An Objective Instrument for Studying Affect and Interaction in ASD. D. K. Bone*, C. C. Lee, M. P. Black, M. E. Williams, S. Lee, P. Levitt and S. Narayanan, *University of Southern California*

Background: Acoustic features of speech are influenced by the speaker's internal emotional state. In particular, emotional arousal is strongly reflected in certain prosodic cues: pitch, intensity, high-frequency energy, and speaking rate (although these can also be consciously altered for socio-communicative purposes). We have developed a robust tool (published) that automatically captures relative changes in vocal arousal over time from a person's speech data. The tool is inspired by a multitude of empirical evidence, further backed by psycho-motor theory; for example, a person's pitch is expected to increase when experiencing fear (high arousal) because the laryngeal folds will tighten as a sympathetic response. Autism spectrum disorder (ASD) research regularly focuses on prosody and affect as behavioral markers. Therefore, we propose multiple uses of this tool for affective and interactional study in ASD.

Objectives: In order to demonstrate the utility of the tool in ASD research, we will conduct three experiments. In the first, we analyze how children with varying degrees of social-communicative difficulties and the interacting psychologists

(clinicians) express affect during activities that impose different social loads on the child. In the second experiment, we analyze how an interacting child and psychologist influence one another as implicated by arousal temporal-dynamics. Finally, we propose the use of computational vocal arousal as a means for further analytics (e.g., data selection), which can then be coupled with other data sources (e.g., lexical information, i.e., the words spoken).

Methods: Audio-video data of Autism Diagnostic Observation Schedule (ADOS) Module 3 (verbal, N=28, 5.8-15.0 years of age) semi-structured child-psychologist interactions were collected. Data were first manually transcribed with utterance boundaries. A computational vocal arousal rating for child and psychologist is made for each utterance based on pitch, vocal intensity, and the ratio of high-frequency energy—all in reference to a speaker's baseline. Social-communicative difficulty is defined by overall ADOS severity. Social load was designated on a 5-pt scale for each ADOS Module 3 activity by seven clinicians experienced in autism assessment. Social load was grouped into three levels (*high*, *medium*, and *low*). Correlation and granger causality are used to quantify the mutual influence between participants' arousal. Various measures are considered for behavioral saliency based on vocal arousal.

Results: Initial evidence suggests that the psychologist has higher relative vocal arousal during *high* social demand activities when interacting with children that have greater social-communicative difficulties. This is interpreted with regard to other conversational and turn-taking findings from previous studies within this data. Additionally, we find that children with greater ASD severity are less responsive to changes in the psychologist's arousal. Lastly, we provide examples of other potential uses of this vocal arousal measure.

Conclusions: Vocal arousal as obtained by this freely available tool (currently implemented in Matlab) is a useful measure of expressed emotional arousal. In this work, we show its utility for analyzing arousal compared to social load for child and psychologist, mutual influence of arousal between speakers, and in conjunction with other modalities as a possible measure of behavioral saliency.

**136.213 213** Cultural Contexts in Virtual Environments for People with Autism. M. Habash* and D. J. Moore, *Leeds Metropolitan University*

Background: This abstract reports on the results of a study on the use of home-based intervention program to teach social skills to children with autism, supported by a computerised culture-rich simulated virual environment.

Objectives: The study had the following objectives:

1- How effective was a home-based intervention program in addressing the social deficits of people with autism targeted (social skills and positive social interaction)

2- Were the computerised components successful in facilitating the delivery of the intervention program?

3-Did the attractiveness and prima facie favourable characteristics of the simulated virtual environment; including the culture-contexts improve the study outcomes?

Methods: An quivalent pre-test and post-test single-subject design study with 14 participants diagnosed with autism from the Gaza Strip participated in this study. This region is well-known for severe socio-economic challenges. The study involved confirming the diagnosis of autism and delivering a home-based intervention program based on discrete trial teaching to the participants. The study utilised quantitative and qualitative data collection measures

Results: Results suggest that a computerised supplimentaty program was beneficial in deliverying the intervention program and that the participants shows improvements in their social skills and increase in their positive social interactions

Conclusions: Results suggest that cultural contexts within computerised programs are benifical to participant with autism. Findings also report on study challenges and issues related to use of technology in 3rd world setting; diagnosis issues; translation of instruments issues, and access to intervention programs

**136.214 214** Design and Preliminary Assessment of a Virtual Reality Driving Environment for Adolescents with ASD. J. W. Wade*[1], D. Bian[1], L. Zhang[1], A. Swanson[1], M. S. Sarkar[2], Z. Warren[1]

and N. Sarkar[1], (1)*Vanderbilt University*, (2)*Middle Tennessee State University*

Background:

Adolescents and young adults with ASD often display potent impairments in metrics of adaptive outcomes and functional abilities (Shattuck, Narendorf et al. 2012). While much of ASD intervention literature focuses on ameliorating social communication deficits and diminishing challenging behaviors, less work has been paid to specific programs targeting focal aspects of adaptive skill development (Palmen, Didden et al. 2012). Independent driving is often seen as an important skill for optimizing functional adaptive independence and enhancing quality of life. Research suggests driving presents a substantial challenge for many with ASD (Cox, Reeve et al. 2012), including different gaze patterns and physiological responses within driving environments (Reimer, Fried et al. 2013).

Objectives:

In the current work we present the design and preliminary application of a novel virtual reality (VR) designed to improve driving skill in individuals with ASD. The VR system was designed to gather data regarding performance, gaze, and physiology in real-time and ultimately via data fusion algorithms to make decisions regarding alteration of tasks to enhance learning.

Methods:

The VR environment was developed using CityEngine and Maya for 3D-modeling and Unity for interactivity. The user interface for the driving simulator consisted of a Logitech G27 controller and a playseat. We used a Tobii X120 remote eye-tracking device to obtain participants' gaze information (e.g., blink rate, fixation duration, as well as the x-y coordinates of the gaze position) and log specific regions of interest (ROI). Participants' physiological signals were collected using a Biopac MP150 physiological data acquisition system and a program developed in MATLAB recorded the data at a sampling rate of 1000 Hz. The game consisted of a set of levels of increasing difficulty during which the participant performed some driving task (e.g., braking, turning at light). Difficulty was manipulated in various ways including increasing the number of vehicles in the environment, increasing the aggression level of other vehicles, and decreasing the responsiveness of the steering wheel. A small pilot study was carried out with five pairs of age-matched teens (between 13 to 17 years of age) with ASD and controls participating in a single 90 minute session with the system.

Results:

A comparison of participant groups indicated (1) the ASD group clearly reported experiencing a higher level of frustration and difficulty than the TD group, (2) there are significant differences in gaze duration time for particular ROI between both groups within the environment (e.g., looking at different targets of environment), and (3) the ASD group failed trials more frequently than the TD group and spent more time overall completing the trials.

Conclusions:

VR systems may represent important intervention platforms for targeting important areas of skill not readily approachable in naturalistic environments without substantial risk of harm (e.g., driving). VR systems capable of responding not just to performance, but important differences in physiology and gaze pattern may be particularly promising. We will present our preliminary gaze contingent VR driving simulator along with the current data.

**136.215 215** Designing Everyday Activities, Living Environments for Adults with Autism. K. L. Gaudion*[1] and E. Pellicano[2], (1)*The Helen Hamlyn Centre for Design*, (2)*Centre for Research in Autism & Education, Institute of Education*

**Background:**

Everyday activities such as doing laundry, cooking a meal or operating electrical appliances help us to develop life skills, live independently and keep our homes clean and enjoyable to live in. Research has consistently found that such everyday activities may present challenges for people with autism. Sensory sensitivities in particular may impact a person's experience and perception of both everyday objects and the physical environment in which the activity is to be performed.

**Objectives:**

Our objective was to expand our understanding of how people with autism perceive and experience

everyday activities at home. We also sought to examine ways in which design might be used to adapt those activities – and the domestic objects associated with them- to make them more enjoyable and educational in terms of personal development and encourage meaningful interactions between people with autism and support staff.

**Methods:**

The research took a people-centred design approach. Twenty adults with autism with limited spoken language and additional intellectual disabilities to express how they perceive and experience everyday activities at home participated, with the help of support staff. Participatory observation, interviewing support staff and encouraging them to record their own observations were also priorities in the study. Co-design workshops, visual sensory profiling cards and visual mapping tools called 'Object of Everyday Use' and 'Doing Things with Things' were also developed to tease out personal responses to designed objects and their related activities. The aim of these methods was to gain insights that might encourage support staff, family members and designers to consider ways of extending, tailoring or otherwise modifying the appeal, function and experience of everyday objects.

**Results:**

The initial research revealed that a person's choice of everyday activity is heavily influenced by their sensory preferences (e.g., watching bubbles) and a person's special interests (e.g., Thomas the Tank Engine). We therefore designed a prototype for a vacuum cleaner and washing machine to illustrate how people with autism can be motivated to become more actively engaged within their own homes by extending and correlating their sensory preferences and special interests, and embracing the way a person likes to do things. In a multiple-baseline design, we are investigating whether the introduction of these new everyday objects yields (a) an increase in the frequency with which they take part in these activities – with the new object and with reintroduction of the old object; and (b) more meaningful interactions between people with autism and support staff.

**Conclusions:**

This holistic design-led approach was successful in eliciting the views, preferences and everyday experience of individuals with autism with limited communication and additional intellectual disabilities. The results will be used to create a design guideline that provides practical ideas on how to re-design or adapt everyday objects and offer advice on identifying such objects with regards to how well they might meet the individual needs and interests of people with autism.

**136.216 216** Developing Software to Support Metacognition in Autism Spectrum Disorder. M. Brosnan*[1], H. Johnson[2] and B. Grawemeyer[3], (1)*University of Bath*, (2)*U*, (3)*London Knowledge Lab, Birkbeck College, University of London*

Background: Metacognition comprises of at least two components - metacognitive knowledge (e.g. 'I am better at multiplication than division') and metacognitive monitoring (e.g. 'I do not understanding this question'). Metacognition has been found to be a powerful predictor of learning performance. For example, research has highlighted that metacognition predicts mathematical performance more powerfully than intellectual abilities and there is extensive evidence that developing metacognition is an effective intervention for students. Research has suggested that weaknesses in metacognition in students with Autism Spectrum Disorder (ASD) can result in a failure to correctly recognise when they have made errors, which can impede learning.

We have developed a computer-based mathematics tutor which incorporates a metacognitive component called an 'Open Learner Model (OLM)'. The OLM was designed to show students their own learning trajectories so that they were made aware of which strategies they had adopted and which were successful - thus aiding in their reflection and future learning. The OLM governs the personalisation of learning by guiding how the tutor dynamically adapts both tuition and assessment for individual students. The OLM supports metacognition by allowing students to access an external representation of what they have and have not successfully achieved and to discuss this with teachers and peers.

Objectives: Demonstate system with findings.

Methods: Our project worked with students through a process called 'Participatory Design', which involves the end-users in the design of the tutor. Students informed how the OLM should look and change as their knowledge states changed.

We monitored the performance of 27 students (aged 11-14) with ASD who were underperforming at mathematics. The students were working at a level of 9-11 year olds and a group of thirty 10-11 year olds were recruited as controls. All participants undertook three 20-minute sessions on consecutive days. At the beginning of each session, students were asked to access the OLM and the representation explained. Each session retained the data for each student, so, for example, the OLM at the start of session two was as it had been left at the end of session one. Students undertook a series of modules within the 'Number' topic of the UK National Curriculum for Mathematics (e.g. multiplication questions). Students could access the OLM any time. OLM access and performance upon mathematics questions were monitored by the system.

Results: The technology demonstration will highlight how the OLM was designed by students with ASD. On average, 139 questions were answered correctly and the OLM was accessed 6 times. The difference in the number of correct responses between session one and session three significantly correlated with the number of times the OLM was accessed. This was the case for students with and without ASD.

Conclusions:

Metacognition can be effectively supported by this software. Although designed by students with ASD the benefits extend to those without ASD. The most revealing data is illustrated by individual learning progression diagrams (e.g. showing getting questions wrong, accessing the OLM and then getting questions correct). These diagrams will be presented alongside the technology demonstration.

**136.217 217** Enhancing Conflict Negotiation Strategies of Adolescents with High Functioning Autism Spectrum Disorders through Technology Supported Collaboration. M. Hochhauser*, P. L. Weiss and E. Gal, *University of Haifa*

Background: The recognition that enhancement of conflict negotiation strategies for adolescents with High Functioning Autism Spectrum Disorder (HFASD) may improve their communication and socialization abilities has heightened the need for pursuing alternate methods of intervention. This study was driven by constructivist learning theory which emphasizes the benefits of training in an environment that promotes learning by experience, collaboration and self reflection. A computer application for video self modeling (VSM), "CONTACT" (Conflict Orientation and Negotiation Training among Children and Teens), was designed so that adolescents with HFASD may practice negotiation strategies to improve their conflict resolution skills.

Objectives: To examine the effectiveness of a 6 week intervention program in which "CONTACT" was used to enhance the negotiation strategies of adolescents with HFASD by means of collaboration during meaningful situations of conflict.

Methods: Adolescents with HFASD, aged 12-18 years, were randomly divided into an intervention group consisting of 18 pairs of participants, and a control group consisting of 25 participants who did not receive any intervention. All participants completed two conflict questionnaires which measure adolescent conflict resolution styles: CONFLICTALK and the Five Factor Negotiation Scale (FFNS). Both within group (pretest versus posttest versus one month follow-up) and between groups responses were compared. The intervention consisted of six 60-minute sessions given over a period of 6 weeks and divided into an experience phase and a learning phase. During each session two conflict scenarios were viewed by pairs of participants according to an ascending order of conflicts of increasing social and emotional complexity. When needed, the moderator used verbal prompts or software application support to scaffold the intervention. During the experience phase, the participants used video self modeling to role play their own responses. These were recorded for the purpose of self reflection to practice and internalize adaptive negotiation strategies. During the learning phase, they were asked to choose a confrontational, submissive, or compromise-oriented response to the presented conflicts.

Results: The results for the FFNS showed that there was a significant improvement in *Communication* for the intervention group in comparison to the control group between pre-test

and post-test, $F(1, 59) = 7.77$, $p = .007$, which was maintained at follow-up, $F(1, 59) = .00$, $p > .05$. In addition, the intervention group reported greater negotiation skills at post-test, $F(1,59) = 7.91$, $p = .007$, than the control group, which was maintained at follow-up, $F(1, 59) = .00$, $p > .05$. The results for the ConflicTalk questionnaire showed that there was a significant improvement in *Problem Focus* for the intervention group in comparison to the control group between pre-test and post-test, $F(1, 59) = 7.24$, $p \leq .001$, which was maintained at follow-up, $F(1,59)= .29$, $p> .05$.

Conclusions: A technology-based interactive platform that is grounded in constructivist learning theory appears to be an effective tool for enhancing conflict negotiation strategies of adolescents with HFASD in situations of social conflict.

**136.218 218** Evaluation of the Use of Mobile Video Modeling for Job Interviews. K. Nguyen*[1], V. E. Custodio[1], R. Weiner[1], R. Ulgado[2], A. Waterhouse[3], L. O'Neal[4] and G. R. Hayes[1], (1)*University of California, Irvine*, (2)*University of Washington*, (3)*Amazon*, (4)*Irvine Unified School District*

**Background**: The acquisition of new skills through observational learning and modeling can account for natural acquisitions in behavior . For individuals with autism spectrum disorder (ASD), research has shown that video modeling, can assist in learning and retaining positive behaviors. Video modeling involves watching recorded videos of others (peer modeling) or oneself (self modeling) modeling positive behavior or successfully completing a task. However, video modeling has mostly been limited to stationary applications that involve caregivers presenting workshops and displaying the videos through television sets.

The ubiquitous nature of mobile technologies provides an opportunity to make video modeling more connected to the activities people are trying to accomplish. Thus, we designed and developed a mobile iOS application, VidCoach, which allows individuals to watch peer model videos as well as record their own videos for self-evaluation and improvement. Initial videos focused on job interview skills for high-functioning students in transition programs. This technology demonstration and poster will include demonstration of the working VidCoach application and results from an empirical study of its use with 14 students in a transition program.

**Objectives**: Design and implement a mobile application that incorporates both peer and self video modeling for individuals with ASD to retain valuable social and life skills, such as successfully interviewing for jobs. Conduct a pilot study to understand usability and usefulness of application as well as efficacy in improving job interview skills for students transitioning to the workplace.

**Methods**: We used an iterative process for designing and developing VidCoach involving observations of transition classes and semi-structured interviews with professionals and caregivers of individuals with ASD. Our study involved 7 students in the intervention group with access to VidCoach and 7 students in the control group without access. We conducted qualitative one-on-one research interviews and organized 2 mock job interviews with local employers before and after the one month long intervention with all the students. We also extracted app usage data from the intervention group after the study.

**Results**: Students from the intervention group indicated that the app was easy to use with minimal training. They revealed greater comfort with interviewing after practicing using the application. Many used the application as a tool to practice with another person to receive direct guidance and or to share their videos for critical feedback. Quantitative data from mock interviews and app usage is currently N/A and in the process of being coded.

**Conclusions**: We have designed and developed a video modeling application that is now available for public download in the app store. The application is most useful for individuals with ASD when used and shared with another person; future development will include sharing features to promote self accomplishment and feedback. We will make further quantitative conclusions to measure improvement in job interview skills after finalizing coding data.

**136.219 219** Experimental Evaluation of a Parent-Implemented AAC Intervention Protocol for Children with Severe Autism. O. Wendt*, C. Masters, N. Hsu, M. Tan, K. Simon and K. Warner, *Purdue University*

Background:

Two popular interventions in augmentative and alternative communication (AAC) for prelinguistic children with autism are picture exchange communication system (PECS) and speech-generating devices (SGDs). Research demonstrated positive effects on functional communication when these two strategies were combined (Boesch et al., 2013). Furthermore, AAC interventions can be implemented by clinicians or parents. Parent implementation shows benefits, and parent involvement is considered crucial in autism intervention (National Research Council, 2001).

Objectives:

This study aimed to answer: (a) what effects does a parent-implemented intervention have on developing functional communication skills and natural speech development; (b) to what extent can parents implement AAC intervention with high fidelity; and (c) to what extent are parents satisfied with intervention procedures and effectiveness?

Methods:

A multiple probe design across participants evaluated treatment effects of the parent-implemented intervention. The protocol contained the first five phases of the PECS approach, followed by generalization and maintenance phases. Dependent measures were: (a) The number of correct requests during a 20-trials session; and (b) the number of vocalizations or word approximations. Intervention phases targeted requesting for food; generalization probes were taken for requesting toys.

Materials included an iPad equipped with SPEAK now!, a sensory-friendly autism app designed to mimic PECS. Parent-training included video resources, written instructions, modeling, role-play, and review of video-taped sessions with feedback.

Inter-observer agreement (IOA) for dependent measures and treatment implementation was established by re-scoring 40% of all sessions. Mean IOA was 99% for requesting, and 92% for emerging speech. Treatment integrity ranged from 82- 98% across parents.

Results:

Children 1 and 2 mastered all five phases of the parent-implemented training, whereas child 3 only achieved phase 3. Acquisition rates varied across subjects, with children 1 and 2 needing on average 6 sessions to master each phase, and child 3 needing 7 sessions. The largest gain appeared when requesting was targeted: For child 1, requesting improved from a baseline mean of 0.25 to a maintenance mean of 17.75; for child 2 from 1.1 to 17.5; and for child 3 from 0.6 to 11.3. All three participants showed generalization to untrained items. Effect size estimates indicated a "highly effective" intervention. Results differed for emerging speech: whereas child 1 made noticeable gains from a baseline mean of 16 to a maintenance mean of 24 word utterances, moderate gains were observed for child 2 and no gains for child 3. Effect size scores were "fairly effective", and "ineffective", respectively.

Conclusions:

Results suggest parents can implement an iPad-based AAC intervention with sufficient fidelity. Children may not be able to complete all protocol phases, and performance may vary with level of intellectual impairment. Treatment effects are most noticeable for requesting skills. A facilitative effect on natural speech development seems most likely for participants with some pre-treatment speech ability. Although these speech effects may seem negligible, such patterns are consistent with previous PECS research. Results underscore the potential of including parents for maximizing benefits of AAC intervention in autism. Practitioners should recognize the value of joint parent-professional partnerships, and develop expertise for parent training.

**136.220 220** How Easy Are Children to Engage during Child-Adult Play? Using Electrodermal Activity As a Marker. J. Hernandez*[1], I. Riobo[2], A. Rozga[2], G. D. Abowd[2] and R. W. Picard[1], (1)*Massachusetts Institute of Technology*, (2)*Georgia Institute of Technology*

Background:
Measuring the attention level of children during social interactions can assist with the identification of developmental delays such as those present in people diagnosed with Autism Spectrum Disorder. Although research has shown that physiological measures map onto observable behavior in the context of attention, this has rarely been studied in young children during live social interactions. The availability of modern

wearable physiological sensors provides an opportunity to automatically monitor not only outwardly sensed behaviors but also physiological states that help study social-communication development early in life.

Objectives:
This work explores whether we can successfully leverage modern biosensors to recognize how easily children engage with adults during social interactions by focusing first on typical development. In particular, we explore the utility of electrodermal activity (EDA) within 31 child-adult interactions. Furthermore, we explore the recognition value of several standard features extracted from the child's EDA responses, and several other features capturing the physiological synchrony of the dyad.

Methods:
Child-adult dyads wore Affectiva QTM EDA sensors on the left wrist during a short social interaction (3-minute on average) in which the adult engaged the child in several activities such a rolling a ball back and forth, and tickling. For each of the activities, the adult rated the child's engagement, ranging from 0 (easy to engage) to 2 (difficult to engage). The final subset of data consisted of 31 sessions of typically developing children (14 females) with an average age of 21 months (SD = 4.9). The sample was divided into: 1) easier to engage (n = 17), consisting of children who scored zero on all activities; and 2) harder to engage (n = 14), consisting of the children who scored 1 or 2 for at least one of the activities. These groups were used as classes to be recognized in a binary classification problem with Support Vector Machines. EDA responses from both the child and the adult were normalized and decomposed into tonic and phasic components. Several features characterizing the general activation of the child (e.g., number of peaks) as well as the physiological synchrony of the dyad (e.g., correlation) were used for the analysis. Forward Feature Selection was used to select the most discriminative features.

Results:
The average intensity of the peaks of the phasic component of the child was the most discriminative single feature in automatically differentiating the two groups, yielding a classification performance of 80.2%. Among several features that captured the physiological synchrony between the child and adult, the Pearson Correlation between the tonic components achieved a classification performance of 70.5%. Finally, the combination of standard features extracted from the child's responses and features capturing the physiological synchrony of the dyad yielded the highest classification performance, 97.2%.

Conclusions:
Measurements of child physiology and its synchrony with the adult's physiology enabled high discrimination between observed ratings of engagement levels provided by the adult. Our findings represent an important first step towards providing new measures to reliably and objectively quantify social behavior, an important advancement for the study of child development.

**136.221 221** Impact of Collaborative Ipad Game on Joint Engagement for Children with Social Skills Deficits. L. E. Boyd*[1], G. R. Hayes[2], H. Fernandez[3], M. Bistarkey[3] and K. Ringland[2], (1)*North Orange County SELPA*, (2)*UCI*, (3)*La Habra City Schools*

Background: The need for evidence-based research on technology for students with autism is paramount. Joint Engagement often requires the support of adults. The iPad provides a cost effective and mobile opportunity to address this core deficit.
Objectives: This study investigated the impact of a collaborative computer game (Zody) on joint engagement on pairs of children with autism spectrum disorder.
Methods: Six children with moderate to severe characteristics of autism were paired in 15 minutes sessions during a rotation of social skills instructions during school. This study involved a full reversal treatment design using a non-technical activity for pairs (Build Lego set) as the baseline condition and Zody, a collaborative iPad game designed to teach the core social skill needs of students with autism, as the treatment condition. Joint engagement was measured by direct observation. A momentary time sampling technique was used to capture the occurrence or non-occurrence of joint engagement at 10 seconds intervals.
Results: Results indicate differences between the baseline and treatment conditions as well as generalization of treatment effects to the low structured condition.

Conclusions: Computer and video games can be used to encourage joint engagement in children with social skills deficits, particularly those with autism. However, additional design considerations should be taken into effect in future technologies, and larger-scale clinical trials should be conducted to validate these results.

**136.222 222** Iterative Design of a System to Support Diagnostic Assessments for Autism Using Home Videos. N. Nazneen[1], A. Rozga*[1], C. J. Smith[2], R. M. Oberleitner[3], G. D. Abowd[1] and R. Arriaga[1], (1)*Georgia Institute of Technology*, (2)*Southwest Autism Research & Resource Center*, (3)*Behavior Imaging Solutions*

Background: Direct observation remains a gold standard practice in diagnosing ASD. While clinical professionals acknowledge that observing behavior in the natural environment is crucial to obtain an accurate and comprehensive assessment, such observation is currently not feasible to implement into clinical practice on a large scale.

Objectives: To iteratively design a system that will enable parents to record video examples of their child's behavior in the home under the guidance of a clinician, and share these recordings with the clinician for the purpose of diagnostic assessment for autism.

Methods: An initial prototype was developed based on interviews with 11 clinicians experienced in diagnosing autism and 6 parents of children with autism. The system consisted of two components. First is an application installed on a hand-held device that guides parents to record and upload four scenarios of their child that were selected on the basis of eliciting a range of behaviors relevant to diagnosing autism. The second component is a web portal for clinicians to review uploaded videos and tag behaviors relevant to diagnosing autism. If the clinician needs more video information, they can send specific recording instructions to the family. Once all videos are reviewed, the clinician completes a DSM checklist. The initial design was evaluated and improved through two usability studies. In each study, four families of children ages 3-6 years with an autism spectrum diagnosis were invited to a home-like laboratory facility for a two-hour session to record the four scenarios using our system. All families were interviewed about their experience using the system. In the second usability study, the 16 videos recorded by the four families were reviewed by a clinician to rate their utility for the purpose of diagnostic assessment.

Results: The videos recorded by parents, along with interview transcripts, were reviewed to identify specific capture challenges. In the second usability study, 33% of the parent-recorded videos were rated as appropriate for conducting an autism diagnostic assessment by the clinician, while another 47% were rated as partially useful but requiring additional exemplars. The parameters that affected the clinical utility of parent-recorded videos can be broadly categorized under *staging* (e.g. camera positioning and environmental setup) or *social presses*(e.g. frequency and type of interactions with the target child).

Conclusions: Using our system, parents were able to record examples of their child's behavior that were rated as clinically useful in evaluating for signs of autism. However, it is clear that clinicians need to be able to send specific instructions to guide parents during the in-home collection process to maximize the clinical utility of the recordings. Based on our findings we developed a set of recording instructions and embedded them within the capture application. We are currently conducting a study in which families of children recently diagnosed with autism will use our system in their homes, under the guidance of a remotely-located clinician. Two clinicians will independently review the videos uploaded by each family and complete a diagnostic checklist for autism, which will be compared to the child's current diagnosis.

**136.223 223** Ka-O-TV: An Eye Gaze Detector for Early Diagnosis of ASD Phenotype. T. Haramaki*[1], K. J. Tsuchiya[2], R. Nakahara[2], M. Wakuta[1], K. Suzuki[2], N. Mori[2] and T. Katayama[1], (1)*Osaka University United Graduate School of Child Development*, (2)*Hamamatsu University School of Medicine*

Background:

A range of questionnaires have been invented to detect young children with autism spectrum disorder (ASD), but they rely on caregivers' recall and/or non-expert assessment. Furthermore, they are time-consuming and appear psychologically intrusive for some caregivers, making their responses somewhat biased. Objectivity of the responses therefore may be compromised.

A novel technique, eye gaze detector, provides us objective and useful findings that may be associated with early phenotypes of ASD. Unfortunately, the technique has still not been well founded largely because of limited availability of the devices, difficulty in calibration for very young children, and low data retrieval rate. To challenge these limitations, we invented a new eye gaze detector, "Ka-O-TV", with the technical assistance of Prof. Yoshinobu Ebisawa, Shizuoka University, Japan.

Objectives:

1. To investigate data retrieval rate of Ka-O-TV with a sample of consecutive 1:6- to 2-year-old children.

2. To investigate whether Ka-O-TV successfully differentiate those with and without potential diagnosis of ASD.

Methods:

Participants are representative 1:6- to 2-year-old Japanese children who attended at public health checkup sites held every month in Saga-city, Japan. By the time they were examined with Ka-O-TV, none of the participating children has been confirmed or suspected to have a diagnosis of ASD. Ka-O-TV devices used in the present study were manufactured by JVC Kenwood Corporation. Nice features of the device include the fastest- and easiest-ever calibration; it only takes 5 seconds although effortful attention to the calibration screen is not necessary. Ka-O-TV provides a series of visual stimuli, which have been designed to attract young children at this age and to illuminate social eye gaze features of ASD. It takes less than two minutes to complete the whole process of the presentation of the visual stimuli. Assessment of ASD phenotype was conducted with M-CHAT (Robins et al., 2001) for all the children and with ADOS (Lord et al, 2000) as a part of their full clinical assessment after the health checkup.

Results:

We examined 169 children (M:F = 97:72, age: 19-26 month old). Average data retrieval rate of these children was 0.84. Whilst most children achieved the data rate of >0.90, 9 children (5%) showed the rate lower than 0.50.

Two sets of visual stimuli (preferential looking) were shown to be highly correlated with M-CHAT total scores. The two sets also discriminate children with ASD, confirmed clinically and with ADOS in some children, from those without ASD. The combination of the two stimulus sets provided sensitivity of >90% and specificity of >80%.

Conclusions:

Ka-O-TV was shown to retrieve eye gaze data, quickly and successfully, from representative young children. It also successfully differentiated those with and without an increased risk of ASD.

**136.224 224** Live Internal State Interaction Monitor Using Google Glass + EDA. I. Riobo*[1], A. Parnami[1], J. Hernandez[2] and G. D. Abowd[1], (1)*Georgia Institute of Technology*, (2)*MIT Media Lab*

Background:

One core competency in establishing any successful social interaction is being able to adequately self-regulate and co-regulate our internal emotional arousal as we interact with other people in any given context. As two neurotypical (NT) individuals engage in any interaction, both can externalize, regulate their own emotional arousal levels as well as identify the internal state of their communication partner as the interaction goes on. This co-regulation process happens naturally and both partners modulate their internal state as the social interaction occurs. This is not the case when interacting with individuals on the autism spectrum, because of the challenges they have in communicating intentions or desires as well as externalizing their internal state. Furthermore, maximizing the communication flow as well as helping the individual with autism regulate entails the ability to read their internal state, which requires a considerable amount of time and training. This learning process is extremely costly to individuals with autism as well as all the people involved in their daily lives.

Objectives:

We are exploring the potential benefits of making visible the internal state of individuals with autism as a clinician, therapist and / or parent interacts with that individual. In particular, we are leveraging the combination of comfortable, ambulatory and non-obtrusive Electrodermal

Activity (EDA) biosensors with the Google Glass, in order to provide live feedback of the emotional arousal level of the individual with autism as the interaction occurs in any given context.

Methods:

Our demonstration uses Affectiva Q$^{TM}$ Electrodermal Activity (EDA) sensors at 32Hz on either the wrist or the ankle of a child with autism, which will transmit wirelessly the raw EDA data to the Google Glass worn by an adult interacting with the child. The Google Glass processes and applies validated physiological filters to the raw EDA data in order to remove noise and make it meaningful to the adult as they interact with the child in any given context. As the adult engages the child, she will be able to use the Google Glass to annotate events of interest. The video, EDA data, and annotations will be transferred to a laptop enabling clinicians, therapists and / or parents to review, reflect and analyze in more depth these pre-annotated events of interest.

Results: N/A

Conclusions:

We hope this demo will provoke two opportunities. First, this technology might be used to gain deeper insights into the autistic experience in social interactions. Second, this approach could make it easier for an adult to learn how to best interact with a child by "seeing" how the child reacts to their social advances in a given environment.

**136.225 225** M-CHAT. J. Hawthorne*, *Prometheus Research, LLC*

Background: The M-CHAT-R/F (Modified Checklist for Autism in Toddlers, Revised, with Follow-up) is the newly-revised version of a widely-used screening questionnaire. The M-CHAT is used by health professionals to identify toddlers between 16 and 30 months who present a measurable risk for Autism Spectrum Disorder. The screener has traditionally been administered in paper format, during which a child's parent answers twenty Yes/No questions; depending on the parent's responses to these questions, additional questions are presented in an interview format. A scoring algorithm is then applied to evaluate the child's risk.

Objectives: Build a web application that allows parents to complete the 2-stage M-CHAT-R/F questionnaire online, without an interviewer. The application must be simple enough that a parent can complete the questionnaire without guidance, using any common web browser (on a computer or tablet). It will also be accessible by the child's doctor, who can review the results and discuss them with the parent. Parents will have the option to complete the questionnaire at home or at the doctor's office, with the assurance that their data will remain private and visible only to their child's physician and to research staff. Parents choosing to complete the form at home will have the option to exit and return later to continue where they left off. The child's doctor will be able to submit an opinion about whether the child may have ASD, and research staff will be able to review this data (along with the questionnaire results) and contact children who are candidates for further screening. Parents will have the option to complete an M-CHAT-R at their regular 18-month and 24-month office visits.

Methods: Prometheus programmed a web-based version of the 2-stage M-CHAT-R/F, incorporating the logic that determines which questions are asked and the algorithm that determines the child's score. Prometheus then built an application that allows a parent to enter contact information, demographic information about their children (who are of qualifying age), and finally the M-CHAT-R/F itself. When the parent completes the questionnaire, the child's doctor accesses the scores via a separate application, the "Doctor's Portal." The doctor completes a "Clinical opinion" form, which is visible to researchers (who have access to all data). The application makes another M-CHAT-R/F available for the child five months after the previous one is completed (assuming the child is still under 30 months old).

Results: Dr. Robins launched the application at five clinics, with plans to expand to about a dozen more. In the first month of active data collection, 38 questionnaires were completed.

Conclusions: The M-CHAT-R/F can be administered over the web in a way that is secure and that allows doctors to participate in the assessment of ASD risk. The questionnaire is simple enough for parents to complete quickly, without a trained interviewer.

**136.226 226** New Software for Prosodic Assessment: PEPS-C with Automated Analysis. M. Filipe*, D. Freitas and S. Vicente, *University of Porto*

Background: Prosodic systems (prosodic structure, intonation, rhythm) play a key role in spoken language. They mediate the phonetic substance of speech within a wide range of communicative functions. The study of prosody has to do with the comprehension and production of the organizational structure of speech, including the patterns of intonation, timing, prominence, and chunking of spoken utterances. Difficulties with these abilities can dramatically influence daily conversations, social and professional interactions, and even typical language development. Although, prosody has been long considered an important topic of research in clinical populations, and it is consensual that atypical prosody is a common feature of autism spectrum disorders (ASD), no consensus has emerged on the characterization of the prosodic profile in ASD.

Objectives: As many studies of prosody in ASD present methodological issues related with the assessment of prosody (e.g., McCann & Peppé, 2003), we aim to improve this assessment through the evaluation of both expressive and receptive prosodic skills using a comprehensive prosodic battery and automated acoustic analysis.

Methods: We used a computerized version of the Profiling Elements of Prosodic Systems – Communication (PEPS-C, Peppé & McCann, 2003) for Portuguese speakers and we included new functions for automated assessment of prosody. The available PEPS-C is a test addressing receptive and expressive skills in parallel. The tasks are at two levels: formal ($n$ = 4) and functional ($n$ = 8). The formal level assesses the auditory discrimination and voice skills required to perform the tasks, whereas the functional level evaluates four communicative domains: (1) Turn-end indicates the ability to decide if an utterance is a question or a statement; (2) Affect signals liking or disliking (reservation) regarding food and drink items; (3) Chunking indicates prosodic phrase boundaries skills; and (4) Focus addresses the capacity to emphasize a particular word in an utterance. The new software records the participant's answers and automatically extracts and analyses acoustic parameters from the expressive tasks. Additionally, it is possible to do automated comparative acoustic analyses of speech production in populations with and without prosodic impairments.

Results: This new software simplifies the process of collecting and analysing prosodic data. We intend to do an interactive presentation of this software showing preliminary data.

Conclusions: The use of this comprehensive assessment could have significant clinical implications and improve differential diagnosis and intervention for individuals with ASD.

References:

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**136.227 227** Paralinguistic Event Detection in Children's Speech. H. Rao*, J. C. Kim, A. Rozga and M. A. Clements, *Georgia Institute of Technology*

Background:

Paralinguistic cues convey a lot of information about the affective state of the speaker. From a diagnostic perspective, cues such as laughter and crying have been found to be important markers in the very early detection of autism spectrum disorders (ASD) in children. Children with ASD have been found to have a high proportion of voiced laughter compared to typically developing children (Hudenko et.al. 2009). Infants at risk for ASD have also been found to produce cries with a higher and more variable fundamental frequency or pitch than low-risk infants (Sheinkopf et.al. 2012). The ability to automatically detect such paralinguistic events in a clinical setting would be of great benefit in helping identifying children who are at risk of ASD at an early age.

Objectives:

To use acoustic features and machine learning algorithms to build a speech-based detector that can automatically determine when speech, laughter, and crying occur in an audio recording.

Methods:

Our data is drawn from a larger dataset of over 140 sessions in which toddlers, 15-30 months of age, interacted with an examiner in a brief play session that included rolling a ball back and forth, looking at pictures in a book, and gentle tickling (Rehg et.al. 2013). The toddlers wore a lapel microphone throughout the interaction, and the sessions were coded to identify onsets and offsets of child speech (vocalizations or verbalizations), laughter, and whining/crying. We used audio data from 35 children, which together included 483 speech segments, 49 laughter segments, and 58 whining/crying segments. We used the audio feature extraction tool, openSMILE, to extract 988 spectral and prosodic features from these segments. The most useful features in discriminating speech, laughter, and crying were selected using the information gain criterion and the forward selection technique.

Results:

We developed three binary classifiers to discriminate between speech and laughter, speech and crying, and laughter and whining. The classification of different types of speech segments was done with a support vector machine (SVM) with a quadratic kernel (degree = 2), using 10-fold cross-validation. The accuracy for discriminating between speech and laughter was 80.6%, between speech and whining was 84.5%, and between whining and laughter 86.9%. The features that were common to the three classifiers were pitch, line spectral pair frequencies (resonant frequencies in the vocal tract when the glottis is fully open and closed), and mel-frequency cepstral coefficients (representation of power spectrum mapped to a psychoacoustical scale).

Conclusions:

We have demonstrated reasonable discrimination between speech and paralinguistic cues along with discrimination between different paralinguistic cues. The results are significantly better than chance (50%) and may lead to a clinical setup where large amounts of speech data from at-risk infants could be parsed automatically.

**136.229 229** Quantifying Imitative Behavior Deficits in Children with Autism Spectrum Disorder. H. L. Miller*[1], R. Patterson[1], D. Popa[2], C. Garver[3], C. de Weerd[4] and N. Bugnariu[1], (1)*University of North Texas Health Science Center*, (2)*University of Texas at Arlington*, (3)*Autism Treatment Center of Texas*, (4)*Motek Medical*

**Background**: Individuals with Autism Spectrum Disorder (ASD) experience coordination and gait difficulties, slower speed in timed movements, and reduced balance and postural stability compared to healthy controls. However, the timing of this divergence from the typical developmental trajectory of motor abilities remains unclear. Given the role of imitation in early motor learning, failure to appropriately interpret and mimic another's movements may produce downstream consequences in coordination, particularly with regard to gestures. Children with ASD have difficulty initiating and engaging in imitative behavior, and clinical measures that evaluate imitation rely on observation and categorical data of "yes" or "no" rather than quantifiable assessments of the degree to which movements are atypical.

**Objectives**: We aimed to assess the development of motor function and quantify deficits in imitative behavior in children with ASD.

**Methods**: A cross-sectional longitudinal design was used to investigate development of motor function in 10 children with ASD (ages 2–12). Evaluations of motor functions were conducted quarterly for one year and compared with those of 10 age- and gender-matched typically developing children. Children performed dynamic daily tasks such as pointing, reaching, balance, and walking as they interacted with virtual environments. They also imitated a humanoid robot as he performed gestures such as "waving hello/goodbye" and "fist bump". We used kinematic data and a Dynamic Time Warping algorithm to quantify the spatial and temporal accuracy of imitative behaviors.

**Results**: Children with ASD had significantly higher variability in Center of Pressure compared to controls at all ages. Children with ASD consistently have significantly lower Froude numbers than age-matched controls. The Froude number (Fr) is directly proportional to the ratio between the kinetic energy and the gravitational

potential energy needed during movement and is given by $Fr = V^2/gL$, where V is the average speed of locomotion, g the acceleration of gravity, and L the leg length. These results suggest that development of an adult-like walking pattern characterized by an optimal energy transfer from cycle to cycle takes places at a slower rate in children with ASD. Children with ASD use significantly longer time to successfully point and reach a target resulting in longer "time per target" values ($p<0.5$). This suggests that the coordination of eye-arm movement in order to reach and point to target is delayed in children with ASD. The results of Dynamic Time Warping showed that children with ASD have poorer imitation behavior, as evidenced by higher discrepancy values of imitation based on weighted joint angle contributions, during the dynamic task compared to the control group.

**Conclusions**: Although improvements in motor function are evident in both groups with increasing age, the trajectories for development of balance, walking, and reaching have a different slope (i.e., they develop at a slower rate) compared to controls. During early childhood, specific motor and imitation impairments can serve as markers for screening/diagnosis of ASD. Given the potential influence of visual information processing on successful imitation, we are conducting a follow-up study using mobile eye tracking to assess visuomotor integration in ASD.

**136.230 230** Real-Time Eye Contact Detection System. Y. Liu*[1], Y. Li[1], Z. Ye[1], F. De la Torre[2], A. Rozga[1] and J. Rehg[1], (1)*Georgia Institute of Technology*, (2)*Carnegie Mellon University*

Background: Eye contact is a key cue for regulating social interactions. Eye tracking and behavioral studies have shown that children with autism are less likely to look at eye regions of the face and to use eye contact while engaging with others. Thus, eye contact represents a key variable that clinicians consider when evaluating children for possible signs of autism. However, in the course of such assessments, it may be difficult for clinicians to collect quantitative data in real-time, such as the frequency with which the child makes eye contact. Although automated eye contact detection has been explored in recent years, none of the existing systems can operate in real-time.

Objectives: Our goal is to automatically detect moments of eye contact between two interactive partners in real-time, and quantify these moments across a period of interaction. We will present an interactive demo of our real-time system.

Methods: Our system utilizes commercially-available eye tracking glasses (SensoMotoric Instruments). These glasses record what the wearer sees via an embedded, outward facing camera, while simultaneously measuring the wearer's gaze fixations in real-time. In our proposed use case, an adult wears a pair of eye-tracking glasses while interacting with a child. The video of the child recorded with the outward facing camera is processed with the Omron OKAO vision library and Intra-Face system [Xiong and De la Torre, 2013] to provide estimates of the child's head orientation and gaze direction. By combining this information with information about the adult's gaze fixations provided by SMI, we developed an algorithm to detect moments of mutual eye contact. We evaluated the accuracy of our eye contact detection algorithm in the context of a brief (2-3 minute) table-top interaction between 9 children aging from 15 to 27 months and an examiner. The examiner brought out a number of toys and allowed the child to explore and play with them without explicitly guiding the interaction. Children were seated in their parent's lap. Two human coders used the video recorded by the SMI glasses to mark the onset and offset of each event in which the child made eye contact with the examiner.

Results: We took the union of the eye contact events, which were independently identified by the two coders and used them to compare the human coding to the automated eye contact detections generated by our system. The overall accuracy of our system was 93.5%, with a precision of 63.6% and recall of 69.2%. We note that across the 9 sessions, the average agreement between the two human coders was 75%, and for individual sessions could be as low as 61.2%.

Conclusions: We have developed a real-time eye contact detection system and demonstrated its accuracy in a setting that resembles many of the current screening and diagnostic assessments for autism. In the future, we plan to extend our system to detect a wider range of the child's gaze targets (e.g. to objects). We will also explore

whether our system may be useful in therapeutic settings for real-time feedback.

**136.231 231** Response and Initiative Joint Attention in Toddlers with Autism Spectrum Disorder: An Eye-Tracking Study. L. Billeci*[1], G. Crifaci[1], A. Narzisi[2], G. Campatelli[2], R. Siracusano[1], E. Maroscia[3], L. Ruta[2], C. Calzone[3], G. Tortorella[4], G. Pioggia[1] and F. Muratori[2], (1)*National Research Council of Italy (CNR)*, (2)*Stella Maris Scientific Institute*, (3)*Ospedale Madonna delle Grazie di Matera*, (4)*Universita' di Messina*

Background:

Autism Spectrum Disorders (ASD) is well known only from three years of life and further information seems to be necessary regarding the modality of onset in the first two years. Studies on high-risk detected several evolutionary atypical ability that can be considered precursors of ASD. In particular 'joint attention' (JA) is a crucial ability for the social development of the child. An atypical functioning of JA in ASD is widely recognized. Up to date JA is mainly assessed using clinical evaluations of behaviour. In this Italian multi-centric study, called ALERT, we used eye-tracking to better characterize JA in toddlers with ASD.

Objectives:

To use eye-tracking technology for the evaluation of JA (response and initiative) in toddler with ASD.

Methods:

A sample of 11 ASD toddlers (9M and 2F; mean age: 21.4 ± 1.6 months) was recruited. Two subjects were excluded because they moved too much during the test and so the amount of data was not enough for the analysis. The test involved the use of video sequences (8 s) and gaze behaviour was measured with an eye-tracker (SMI, RED500). The experiment consisted of three tasks: a response joint attention (RJA) and two initiative joint attention (IJA) tasks. In RJA task a woman is between two identical toys and turns her head and eyes to one of the objects (task 1), in the two IJA task the woman maintains direct gaze but in one case one the object activates unexpectedly (task 2), while in the other one the object appears from one end of the frame and crosses the scene (task 3). Different region of interest (ROIs) were defined: person's face, eyes, mouth and body, target object and non-target object. For each ROI the fixation count (FC), the first fixation duration (FFD) and the fixation time (FT) were measured. FC and FT were computed as a percentage of the total.

Results:

In all the 3 tasks FC and FFD were increased for the face with respect to the other ROIs. In task 2 also FT was increased for the face with respect to the other ROIs. No other significant differences were present among the different ROIs within each task. Comparing the different tasks we observed an increased FC in task 2 vs task 1 for target object ($p=0.02$) and non-target ($p=0.03$) an increased FT for target object in task 2 vs task 1 ($p=0.015$) and vs task 3 ($p=0.004$) and an increased FT for non target object in task 2 vs task 1 ($p=0.04$).

Conclusions:

The protocol developed appears effective in characterizing gaze during JA tasks. The children seem to be more attractive by the objects in the task 2 although they do not distinguish so much between the target and other objects. A longitudinal study could allow to better understanding the evolution of JA ability in children with ASD.

**136.232 232** Self-Adjusting Biofeedback with a Dynamic Feedback Signal Set (DyFSS). L. I. Sugarman*, B. L. Garrison, A. E. Hope, S. Jacobs, A. J. Glade and K. L. Williford, *Rochester Institute of Technology*

Background: The diversity found in Autism Spectrum Disorder (ASD) may also be reflected in the autonomic profile of affected individuals, yet there is a paucity of normative data for how their autonomic functioning may differ. It is known that anxiety is highly prevalent in children with ASD, (Baron, Groden, Groden, & Lipsitt, 2006; Kinsbourne, 2011). Autonomic Biofeedback Training (ABT) is a promising treatment for managing anxiety and ASD symptoms more generally (Sugarman, Garrison, Williford, 2013; Yucha & Montgomery, 2008). However, a clinician looking to use ABT for youth with ASD cannot readily predict which autonomic proxies are the most discernable and controllable for a specific user. Clinical encounters would benefit from software that tunes a combination of sensor signals to the best abilities and needs of each

individual patient. We are developing a Dynamic Feedback Signal Set (DyFSS), a strength-based, self-customizing algorithm. It uses four measures of autonomic function: skin conductance, skin temperature, respiration rate, and low-frequency heart rate variability. By creating individualized and intuitive software, ABT can be refined to address the autonomic heterogeneity of youth with ASD, ease the work of the clinician, and create the potential for integration of ABF into interactive games and media.

Objectives: To test the feasibility and receive input from potential users with ASD regarding (1) a novel biofeedback algorithm that combines four autonomic signals for a unified display interface; (2) a 5-session weekly ABT protocol employing this algorithm; and, (3) parent behavioral observation as an outcome measure for this course of ABT. **Presentation includes a technological demonstration of the current DyFSS prototype.**

Methods: The first version of the DyFSS was tested over 5 weekly sessions of ABT with 10 youth diagnosed by community physicians with ASD. User preferences were obtained by asking participants for direct input and assessed qualitatively. Daily behavior tracking by parents tested for change in ASD symptoms. A questionnaire completed by users at the close of the final session was assessed qualitatively to assess their overall experience.

Results: Initial reactions show that many children are interested in learning more about biofeedback as well as the technology and physiology underlying the process. Some report their use of the skills learned during ABT to cope with stressors in school and at home between sessions. Analysis of parental observation is pending at this time. Areas to improve the current version of the DyFSS include the setup of the physical sensors, customizability of the graphical user interface (GUI), and follow-up to determine whether children continue to use their skills after sessions end.

Conclusions: Youth with ASD are readily engaged through technological interventions such as autonomic biofeedback. It is an effective way to draw interest toward therapy and increase understanding of their physiological processes. It may also decrease their anxiety and associated symptoms. Further refinements of the DyFSS based on input from youth with ASD will improve the relevance of the software in clinical practice and its potential integration into interactive games and media.

**136.233 233** Sensorypaint: An Interactive Surface Supporting Sensory Integration in Children with Neurodevelopmental Disorders. K. Ringland*[1], R. Zalapa[2], M. Neal[1], L. Escobedo[3], M. Tentori[2] and G. R. Hayes[1], (1)*University of California, Irvine*, (2)*Center for Scientific Research and Higher Education of Ensenada*, (3)*Autonomous University of Baja California*

Background: Many children with neurodevelopmental disorders, such as autism spectrum disorder, have sensory processing disorders (SPD), which can lead to inappropriate behaviors and impairments. One therapeutic approach to the kinds of SPD frequently observed in children with neurodevelopmental disorders involves the use of a variety of tools including objects with various textures and tactile sensations, mirrors, and Multisensory Environments (MSE) saturated with visual and audible stimuli and specialized equipment for sensory stimulation. However, children with SPD each have a unique prescription for the amount of stimulation they require for the therapy to be effective. MSE must be physically altered before each child receives therapy. SensoryPaint is an interactive surface with the capability of superimposing the user's reflection on a projected surface and "painting" this surface with balls of different textures and colors, which was designed to augment traditional therapies.

Objectives: We conducted two studies to understand the role of interactive surfaces in support of sensory integration: one in the lab and one as an integrated part of existing sensory therapy. These studies focused on uncovering the potential of this technology to support sensory integration, including stimulus sensitivity, body awareness, motor functioning, and attention and engagement.

Methods: We evaluated the impact of SensoryPaint through two studies: a lab-based study of 15 children with neurodevelopmental disorders in which they used the system for one hour and a deployment study with 4 children with autism spectrum disorder for which the system was integrated into existing daily sensory therapy sessions for three weeks. In the lab-based study, the children played with each of the three modes

of SensoryPaint, in randomized order, for at least 10 minutes each. They were then given the opportunity to play a mode of their choice for an additional 15 minutes. After the final play session, the children were given short interviews about their experience with the system. In the deployment study, video was captured of each session and weekly interviews with the children, parents, and therapists were conducted. All interviews and observations from both studies were recorded, transcribed, and inspected together using a mixed-methods approach. Additionally, we used both deductive analytical approaches based on our initial questions surrounding the potential for SensoryPaint to improve attention and body awareness and inductive approaches, allowing new themes to emerge from our data.

Results: Our results demonstrate that using whole body interactions with an interactive surface can capture the attention of children for whom traditional therapies may not be engaging, augment existing therapies, increase body awareness, improve sensory skills, and promote socialization. SensoryPaint was designed for individual use participants often collaboratively used the interface. As a consequence, children improved their social skills when using the system.

Conclusions: In this work, we designed and developed the SensoryPaint system to explore how interactive surfaces could support occupational and sensory integration therapies for children with neurodevelopmental disorders. Our results indicate that integrating tangible and body-based interactions support existing therapeutic goals and provide novel ways to engage that can promote the development of additional skills and abilities.

**136.234 234** Stakeholder Perspectives on the Utility of a Web-Based Resilience Skills Building Program for Students with High Functioning Autism Transitioning to Postsecondary Education. A. Sam*, D. Childress, K. T. Melillo, I. Coleman and M. DeRosier, *3C Institute*

**Background:** Despite cognitive strengths, individuals with high functioning autism (HFA) pursue college at much lower rates than their typically developing peers. Approximately 24% of individuals with autism spectrum disorder without intellectual disability report no regular educational or employment following high school (Taylor and Seltzer, 2011). Further, when these intellectually capable students pursue college, they tend to drop out prematurely(Glennon, 2001). A growing literature underscores the crucial role of resilience strategies for academic and social-emotional adjustment and persistence in postsecondary education (PSE) (Walton & Carr, 2012). The current lack of well-designed and accessible interventions to help students with HFA transition to PSE contributes to the marked under-education and under-employment experienced by these individuals, which in turn, negatively impacts their overall quality of life.

**Objectives:** To iteratively develop and conduct preliminary testing of a dynamic, customizable resilience and PSE transitioning program, Student Curriculum on Resilience Education for Students with HFA (SCoRE-Propel), designed for unique learning and social-emotional characteristics of students with HFA.

**Methods:** Usability testing of SCoRE and semi-structured interviews were conducted. Students preparing for the entry to PSE or those in programs less than 1 year and their parents (n=12 pairs) reviewed SCoRE in their homes for 2 weeks. The online platform delivers instruction on specific skill domains through a combination of video presentation styles (motion graphics animations, illustrations, and video modeling). Interactive exercises provide individualized feedback and reports based on user responses. After reviewing the program, participants met with research staff individually to give feedback on the usability of the program, and online delivery platform using a 5-point Likert scale (1=Strongly Disagree to 5=Strongly Agree). Participants provided qualitative responses on the program and their understanding of issues related to the successful transition to college.

**Results:** Data analysis is ongoing. Preliminary results show both parents and students found the program components to be of high quality and value as well as a highly usable intervention package (mean ratings > 4). Semi-structured interviews showed that 57% of parents of high school students are unsure how to find resources at colleges, 43% had yet to discuss with their child how or if to disclose diagnosis to college, and 100% had not college finances with child. Parents of college students (100%) thought college personnel do not have enough information on

autism spectrum disorders. Spontaneously, parents most frequently stated independence as a concern (60%). Students most frequently stated performing academically (60%) and social demands (30%) as concerns. Regarding course content, social skills and goal setting were rated the most relevant topics in the course.

**Conclusions:** These data provide evidence for the usefulness and need of the SCoRE program for students with HFA considering PSE. Gathered data was used to create a blueprint of modifications and additions needed to key the intervention to the needs of students with HFA (e.g., new instructional elements, customized graphic design, tailored activities). A subsequent pilot efficacy study of SCoRE for enhancing resilience and transitioning skills needed for successful transition to PSE is underway.

**136.235 235** Stop Frame Coder (SFC): A Tool for Detailed and Reliable Behavior Quantification. K. Libertus*, *University of Pittsburgh*

Background: Several lines of research suggest that there may be subtle differences in motor and social behavior between children later diagnosed with Autism Spectrum Disorders (ASDs) and unaffected peers. In particular, subtle motor delays seem evident during infancy in high-risk infants (Bhat, Galloway, & Landa, 2012; Flanagan, Landa, Bhat, & Bauman, 2012; Ozonoff, Macari, et al., 2008). However, experimental designs focusing on behavioral observations seem more sensitive than standardized assessments in detecting early signs of ASD in infancy (Ozonoff, Young, et al., 2008; Provost, Lopez, & Heimerl, 2007). This highlights the value of detailed behavior quantification and the need for fast and reliable means to quantify behavior in studies on the earliest signs of ASD. When observing behaviors, information regarding social focus, manual engagement, and emotional status are available simultaneously and need to be recorded and scored at the same time. This is not possible using real-time observation approaches, while video-based coding is a long and error-prone process. In this presentation, we introduce the freely available Stop Frame Coder (SFC) software that addressing these issues by using multiple passes combined with frame-by-frame coding.

Objectives: Provide a fast and reliable tool for behavior quantification in the social, emotional, and motor domains to facilitate research on early ASD markers.

Methods: SFC allows observers to score videos frame-by-frame (10 frames/second). Videos are coded in 4 passes to assess visual attention, manual exploration, social behaviors, and emotional state. At each pass, observers focus on a single behavior (e.g., location of eye gaze) to increase accuracy and reliability. Following coding, behaviors coded in different passes can be combined into complex behavior units (e.g., looking at and grasping an object, smiling and looking at another person). A summary and time course output is provided to allow for in-depth analyses of moment-to-moment changes in behavior.

Results: SFC is currently being used by eight different research labs to study infant behavior in diverse domains such as cognition, perception, motor, or social development. Published studies using the coding software have investigated looking preferences in typically developing (TD) infants (DeNicola, Holt, Lambert, & Cashon, 2013), infants' processing and detection of changes in visual displays (Cordes & Brannon, 2011; M. E. Libertus & Brannon, 2010; M. E. Libertus, Starr, & Brannon, 2013; Starr, M. E. Libertus, & Brannon, 2013a, 2013b), and infants' manual exploration strategies (K. Libertus & Needham, 2010, 2011). More recently, SFC has been used to quantify motor behavior in infants at high genetic risk for ASD or children subsequently diagnosed with ASD. Coding samples and results from select studies will be presented along with a live demonstration of the software.

Conclusions: The SFC software allows extraction of detailed motor, social, and emotional behavior in infants and young children. A number of studies have demonstrated its validity and value in research. Use of SFC in studies with infants and children at risk for ASD may shed light on subtle motor and social delays that emerge in early infancy but cannot be detected using conventional methods or standardized screening measures.

**136.236 236** Stories in Motion: A Pilot Study of a Social Visualization and Progress Monitoring Program for Elementary School Students with High Functioning Autism. D. Childress*[1], A. Sam[1], K. T. Melillo[1], T. Henry[2], B. Cassell[1], P. Wood[1], C. Hehman[1] and J. S. McMillen[1], (1)*3C Institute*, (2)*University of North Carolina Chapel Hill*

**Background:** Effective treatments for children with high functioning ASD (HFA) are needed to address the significant social impairments that interfere with their social and peer interactions. Visualization tools such as social stories are frequently used, widely accepted, and theoretically well grounded, but have shown inconsistent empirical support. Computer-based platforms can address this issue by standardizing implementation and enhancing treatment effectiveness. However, most computer-based visualization programs targeted to individuals with ASD have not attempted to establish an evidence-base.

**Objectives:** To develop and test an interactive social visualization and progress monitoring program for elementary students with HFA. With easy integration into classroom environments, Stories in Motion (SiM) has been developed to enhance social skills in students with HFA and document progress toward measurable social goals.

**Methods:** A pilot study was conducted to examine feasibility of SiM implementation, usability in its intended educational setting, and to gather preliminary efficacy data. Participants included 31 triads of students with HFA, service providers, and general education teachers, randomly assigned to participate in either SiM (n=17) or Services as Usual (SAU; n=14). Based on provider rankings of 12 social target areas, students and providers in both conditions completed the 6 target area topics most relevant for the given student. SiM students engaged with the software to create a personalized story (including animated video, comic strip, and highlights card) to be reviewed throughout the week. Data sources included pre/post measures of student global social functioning/behavior, topic knowledge, provider/student ratings of student confidence and frequency of skill performance.

**Results:** Pre-, post-, and follow-up knowledge quizzes for each target area were examined (McNemar's test, test for the equality of two proportions). SiM students showed significant pre-/post knowledge gains for coping, impulse control, and transitioning (improvement = .68, .85, .80, $p < .05$), and long term gains (pre- to follow-up) for anxiety, coping, non-verbal communication, and transitioning (improvement = .76, .78, .9, .73, $p < .05$). SiM students showed significant pre-/post knowledge change for impulse control (Improvement = .83, $p < .05$), and long term gains in conversation, non-verbal communication, sportsmanship, and impulse control topic areas (improvement = .77, .8, .88, .79, $p < .05$). SiM and SAU were significantly different for the bullying and transition topics, during the pretest-posttest interval ($p < .05$). Pretest-follow-up interval results for coping suggest SiM is more effective at increasing knowledge in the long term than SAU (.78 vs .56 improvement, $p = .061$).

Pre/post provider ratings on the Social Responsiveness Scale (SRS, Constantino & Gruber, 2005) showed a reduction in social cognition problems for both groups ($b = -2.85$, $p < .05$). The SiM condition was effective in reducing problems in social motivation, while the SAU was not ($b= -5.308$, $p < 0.05$).

**Conclusions:** These data provide preliminary evidence for the effectiveness of SiM for increasing student social skill knowledge. These findings are particularly strong given our small sample size and the briefness of the intervention period. Additionally, provider and student usability data support utility of the program in educational settings.

**136.237 237** System for Facilitating Model-Driven Behavioral Therapy. R. Jakobovits*[1], R. C. Bocirnea[1] and S. L. Shook[2], (1)*Experiad Solutions*, (2)*Northwest Behavioral Associates*

Background: Evidence-based, early intensive interventions such as the Early Start Denver Model, are based on rigorous, structured curriculums (Dawson et al., 2010; Rogers et al., 2012) and established learning principles and approaches (McEachin et al., 1993). These approaches create individualized treatment plans from libraries of objectives, either formal or informal, that cover a range of domains and clear mastery criteria. Such interventions may be difficult to implement in community settings where therapy is delivered by tutors under the supervision of program managers. Existing therapy management systems do not accommodate the creation of new structured models, importing existing models, or provide ways for supervisors to monitor adherence to such models. Innovative therapy management software is needed to support the adoption of evidence-based approaches and allow therapists to deliver model-driven programs in a wider variety of settings and communities.

Objectives: We are developing a system (Abacus, NIH SBIR 1R43MH098476-01A1, Jakobovits PI), that will allow therapy practice directors to create and import structured models, tailor them to fit their own practice approach, and use them as templates governing the creation of curriculums within their organization. The software will enable program managers to construct and refine individual therapy curriculums based on the proscribed model, and efficiently supervise tutors who will use a tablet app to deliver therapy within the model.

Methods: We are building a prototype which is being evaluated by researchers at the University of Washington Autism Center (UWAC) and community service providers at Northwest Behavioral Associates (NBA). The system consists of four main components: (1) Therapy App: a tablet-based data collection platform that allows tutors to stay continuously connected with the child throughout the session, while at the same time ensuring that all treatment objectives are met; (2) Curriculum Tuner: an online tool for managing individualized curriculums, drawing from shared objectives libraries; (3) Team Dashboard: a web-based solution for monitoring treatment dosage, objectives coverage, and fidelity across practitioners; and (4) Parent Portal: a user-friendly interface for engaging parents as active participants in the structured delivery of the intervention.

Results: We have developed a prototype and are in the process of generating detailed qualitative measurements of the feasibility of 14 key functions of the system. The NBA model (2500 templates) has been imported into the system, and interventionists have begun assessing its functionality. Preliminary findings indicate overall high user satisfaction and ease of use. Functional analysis demonstrates high usability; program managers are able to successfully create tailored treatment plans, and tutors are prompted to move to the next learning step in every instance where mastery criteria was completed. We will present this system and preliminary findings, including results from user surveys and feasibility measures.

Conclusions: Abacus represents a more efficient mechanism for conducting intervention and adhering to a structured models, including user-friendly interfaces for creating, adjusting, and monitoring individualized curriculums, and for performing rigorous data collection and analysis. This new technology has the potential to accelerate the adoption of emerging behavioral interventions and ultimately contribute to the evolution of the field of autism treatment.

**136.238 238** The Development of an Intelligent Virtual Reality Intervention Application. E. Bekele*[1], J. W. Wade[1], D. Bian[1], L. Zhang[1], A. Swanson[1], M. S. Sarkar[2], Z. Warren[1] and N. Sarkar[1], (1)*Vanderbilt University*, (2)*Middle Tennessee State University*

Background: Recent advances in human machine interaction have enabled the use of computer technology (Goodwin, 2008), robot-mediated systems (Bekele et al., 2012, Warren et al., 2013), and virtual reality (VR) based systems (Bekele et al., 2013; Kandalaft et al., Lahiri et al., 2013) for potential use in social interaction and intervention paradigms for individuals with ASD. VR platforms have preliminary demonstrated the capacity to improve social skills in individuals with ASD (Bekele et al., 2013; Kandalaft et al., Lahiri et al., 2013; however, currently utilized paradigms have often been reliant on confederates or modalities (e.g., menu response paradigms) that potently limit the ability of systems to mimic, and potential impact, naturalistic interactions beyond the paradigms themselves.

Objectives: This current work describes the development and preliminary validation results of a multimodal VR interface and a dynamic fusion strategy for incorporating these modes into within system decision making. This system was constructed to be able to measure and respond in real-time to user speech, gaze patterns, and physiological responses.

Methods: Three interfaces were integrated into a VR interaction platform: 1) speech-based turn-taking dialog management, 2) multi-channel peripheral physiological signal detection (Liu et al., 2008), and 3) an eye gaze sensitive module (see Bekele et al., 2013). While the physiological signal detection and eye gaze modules were developed in previous work, this specific research examined the development of speech-based recognition and integration of all three systems into one interactive environment. For the speech interface we developed domain dependent conversation threads for more reliable speech-based recognition. . We also developed a dialog

management engine that parses these threads and perform a lexical comparison between each of the options and what the user utterances as captured from a speech interface module within a specified time interval. Initial validity of these interfaces was tested individually across user studies. Further, the output of the physiological detection algorithm and the gaze sensitive module were assessed during the user performance via multimodal input fusion (Dumas et al., 2009; Jaimes et al., 2007) tested against clinician ratings as a ground-truth for decision making.

Results: Validation results for the dialog management system in terms of the performance of the speech recognition, lexical similarity and overall option selection will be presented and available for real-time demonstration. For the physiological-based affect recognition, we randomly divided the data set in to training, validation and testing sets with proportion of 70%, 15%, and 15%, respectively, for all the classifiers and used 10-fold cross validation to fit the best model in each case. Results of four channel physiological data classification utilize varied machine learning algorithms exceeded 80%.

Conclusions: The current work provides a preliminary demonstration of the ability to develop VR environments and paradigms sensitive to not only performance within systems, but also gaze patterns, physiological responses, and naturalistic speech. The ability to harness such behaviors within future intelligent systems may dramatically enhance VR environments as social intervention tools.

**136.239 239** The Missing Data of the App Phenomena. M. Eckhardt*[1] and R. W. Picard[2], (1)*Massachusetts Institute of Technology, The Media Laboratory*, (2)*Massachusetts Institute of Technology*

Background:

Over the last three there has been widespread adoption of tablet computers. This has been especially true among the autism community with respect to the iPad. The intuitive, touch interface of these devices has made them accessible to children, and allowed children diagnosed with autism to use computational devices in new and exciting ways. Apps that target child education are among the top downloaded apps, and there are numerous autism related websites with extensive list of "apps for autism." Because of the widespread use of tablets with children diagnosed with autism there is a new potential for collecting data at large scale related to usage and learning objectives. Despite this, we have little understanding of their actual usage, benefit, or greater potential for the autism community.

Objectives:

There are many autism related websites that provide lists of apps intended for use by children diagnosed with autism. Of these Apps, very few are intended as "autism" apps and are instead simply apps for children. The vast majority of these apps have informal educational purpose. We wished to better understand what kinds of apps were being suggested and used by the autism community. Furthermore, we wanted to know if the apps were providing data collection of any kind, which may be used for subsequent analysis of usage and or learning.

Methods:

We conducted searches of the internet including personal blogs, educational resource websites, and autism related websites such as Autism Speaks to compile a list of over 400 apps. Each app was reviewed and categorized. In addition, we attempted to determine if individual apps collected usage data and if so if any type of post-analytics was performed.

Results:

The apps were categorized into 10 groupings: communication, language, math, scheduling, daily skills, social and emotional learning, motor skills, self soothing, behavior tracking, and entertainment. Communication and language learning apps accounted for 21% and 24% of all apps. Overall, some 27% of apps collected some type of data at the local device level. Only 9% of apps provided services that stored the data on a remote server for sharing or further analytics.

Conclusions:

In a large review of applications from many sources we found that apps promoted for the autism community fall into 10 general categories. Furthermore, we found that communication and language learning apps account for 45% of all app types. With respect to understanding usage and

learning giving the apps there must first be apps that collect data. We found that only 27% of apps collect any type of usage data, while even fewer provided back useful analytics. Furthermore, only 9% of apps collect data on a remote server for sharing or further analytics. Because of the mass adoption of tablet computers by the autism community, there is an opportunity to learn about behavior and learning through the usage of apps. We have the potential to leverage scale to be understand how those diagnosed with autism use technology, but we cannot do this unless we are collecting data and performing analysis.

**136.240 240** The Use of a Mobile APP Parent Training Program to Improve Functional Communication in Young Children with Autism. G. C. Law*, M. F. Neihart and A. Dutt, *National Institute of Education*

Background:

There is a significant increase in the number of diagnoses of autism spectrum disorder (ASD) in recent years. Evidence-based practices are found to be most promising in improving the functioning of children with autism, however, limited resources and high costs have hindered them from receiving prompt and timely intervention. Communication intervention in early life will impact significantly on long term outcomes of ASD children. Parents are found to be vital and important resources and training them to be therapists will help reduce their cost for intervention. The project is an initial step to test the use of technology to disseminate an evidence-based practice in an effective and efficient way.

Objectives:

The primary purpose of the project is to examine the effectiveness of using a mobile application to train parents to implement naturalistic language intervention so that their young child with autism will improve in their functional communication, especially in requesting objects in their daily contexts.

Methods:

A mobile app was developed for parent training, using the adult training framework of 'Behavioral Modelling Training' to deliver the content of Naturalistic Language Intervention. Parents and their young child with ASD (aged 3-5) were recruited. A pilot study of single subject experimental design was conducted across 3 parent-child dyads. Behaviours of both parents and children were measured during the phase of baseline, training, post training (i.e. parent's intervention on child) and follow up. Social validity, app program acceptability and satisfaction were administered with survey forms.

Results:

Results of the pilot study underway will be reported. Parental gains in knowledge and principles of Naturalistic Language Intervention, their frequency of utilization of the mobile app during the course of parent training will be shared. Changes in target behaviors of both parents and children during and after training will also be reported.

Conclusions:

Results suggest that Mobile applications in behavioural intervention are a promising means for improving efficiency and effectiveness in evidence-based practice Further research is needed to assess generalizability of parent and child gains.

**136.241 241** Using Mobile Technologies in-Situ to Train Examiners in the Behavioral Assessment of Infants and Toddlers. O. Ousley*[1], C. Bridges[2], A. Southerland[2], A. Gupta[2], M. DiRienzo[3], A. L. Pavluck[4] and J. Rehg[2], (1)*Emory University School of Medicine*, (2)*Georgia Institute of Technology*, (3)*Carter Consulting for the Centers for Disease Control and Prevention*, (4)*Task Force for Global Health*

Background:

Examining early social-communicative behaviors during infancy allows the detection of risk for language and social delays, important for the early detection of autism. As recommended by the American Academy of Pediatrics (AAP), our goal is to develop a method for whole population behavioral screening and to develop a method for training non-expert examiners in the rapid assessment of children's social-communication abilities, which may serve as a supplement to parental report. Using a brief 4-minute interactive assessment (i.e., the Rapid-ABC), we have collected preliminary data from a community sample of 125 infants, which shows promising results; however, to achieve population-level screening, we must reduce the cost of personnel

training, improve our ability to disseminate training and assessment protocols, and collect data on a continuous basis to update local, national, and international norms.

Objectives:

The study objective is to implement a mobile technology solution that will overcome the training, data collection, and data management obstacles required for full population screening of infants and toddlers.

Methods:

Subjects: We will present pilot data from a feasibility study conducted at a child psychology research site, and a clinic site that serves children at genetic risk for autism

Training phase: The R-ABC currently exists as a one-page form with an accompanying 13-page training and scoring manual, and requires an extended training process. To overcome training obstacles, we are testing the use of a mobile application (app) to 1) provide R-ABC examiners detailed training, which is time and cost efficient, 2) streamline scoring procedures to minimize disruption of the examiner-child interactions, and 3) ensure accurate and complete data collection. The training app presents task instructions in a sequential manner, provides "help" buttons to explain code definitions, and allows automated scoring.

Data collection phase**:** At enrollment, the child's parent is presented with a consent form on which personal identifying information is entered. Enrollment data is linked to the de-identified examination electronic record through a numeric barcode label on the form which is scanned directly into the electronic survey through the device camera. Once entered, the data are transmitted through an encrypted connection to a secure server, where it can be accessed through a web-based interface.

Results:

This technology, although in an early phase of evaluation, streamlines the processes of training, administration, scoring, and information management. Through a hands-on demonstration, we will illustrate the benefits of mobile technology in the training and administration of the R-ABC. We will also show how data collected "in the field" can be accessed via a dynamic user interface to access data and produce automated reports of individual and group data.

Conclusions:

We conclude that mobile technology innovation provides a solution for training examiners in the field to conduct brief behavioral assessments, and that these innovations can provide a solution for population screening, secure transmission of data, and aggregation and management of large datasets. We also conclude that such a model could be used for behavioral research nationally and internationally.

**136.242 242** Virtual Humans Simulating Joint Attention Based on Real-Time Eye-Tracking. O. Grynszpan*[1], B. HAN[2], M. Courgeon[3], J. C. Martin[4] and J. Nadel[5], (1)*University Pierre et Marie Curie*, (2)*University of Paris8*, (3)*Lab-Sticc / University of South Brittany*, (4)*CNRS/ Université paris-Sud*, (5)*French National Centre of Scientific Research (CRNS)*

Background: The pivotal role of gaze in social interchanges is considered altered in Autism Spectrum Disorders (ASD). Literature reports a diminished propensity to use the gaze of a social partner as a way to derive a representation of her/his mental states. Joint attention has drawn a lot of research interest in the field of ASD. Indeed, the appearance of joint attention behaviors is reported to be delayed in the developmental course of ASD and to predict poor later acquisition of social and communicative skills. Until now, most of the research devoted to assess joint attention competencies has been based on experiments where the participant is expected to follow the gaze of another person (passive joint attention). The active situation where the participant initiates and leads a joint attention episode is much harder to implement as it requires an experimental setup that can detect and react to the participant's gaze.

Objectives: The goal of this project is to devise and evaluate a technology that enables studying gaze leading paradigms. We endeavoured to create a controllable yet ecologically valid experimental setup.

Methods: This project required merging technologies in the fields of eye-tracking and embodied virtual agents.We designed a platform that displays virtual humans endowed with the

ability to follow the user's gaze in real-time. The eye direction of the user is detected by an eye-tracker so as to determine the eyes and head orientations of a virtual human. To test this platform, participants were placed face-to-face with two virtual humans and had to carry out a task that required selecting an object among several choices. We compared two conditions: in the experimental condition, one of the virtual humans was continuously following the direction of the eyes of the participant while in the control condition the gazing behavior of the two virtual humans was independent of the participant.

Results: Technical tests showed that the platform was able to correctly simulate gaze following behaviours. The experimental protocol was administered to 15 typical adults. Eye-tracking data revealed that the experimental manipulation influenced the gazing behaviour of typical participants, even though they were not aware of leading the gaze of the virtual human. Case studies with participants having ASD will be presented.

Conclusions: We developed a novel platform that opens new avenues for studying joint attention in ASD. It provides an answer to the lack of relevant tools enabling to examine active joint attention, which is believed to be the critical component of joint attention impairments in ASD. The eye-tracking data yielded by the platform enables precise analyses of the viewing patterns associated with joint attention. Additionally, this platform holds great potential for assessing joint attention skills and could thus be proposed in the long term for clinical evaluation.

## 137 Adult Outcome: Medical, Cognitive, Behavioral

**137.001 1** Anxiety and Preoccupation in Cases of Autism Spectrum Disorder (ASD) Diagnosed after Age 16. J. Adachi*[1] and T. Uchiyama[2], (1)*Hokkaido University of Education*, (2)*Fukushima University*

**Background:** Some ASD cases show few obvious characteristics during early childhood and first diagnosis as an adult is not uncommon. Delay in the provision of support may then become a problem.

**Objectives:** Investigation of the developmental characteristics of such cases may help to identify early support needs.

**Methods:** The subjects were 41 high-functioning ASD individuals aged at least 16 years and IQ 70 or higher (measured within the previous 3 years) assigned to a Delay Group (19 individuals, average IQ=102.8, average age 30.0 years, male/female ratio = 15:4), where a definite diagnosis of ASD was made after the age of 16, or an Early Group (22 individuals, average IQ=100.4, average age 25.4 years, male/female ratio = 18:4), where this diagnosis, or an observation of maladjustment, was made before age 16. Development was investigated using 1) a developmental history, 2) evaluation of the Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) peak symptoms during infancy and evaluation of current symptoms on the adolescents/adults scale, 3) the Autism-Spectrum Quotient (AQ) Japanese version, 4) Early childhood anxiety scale, 5) Preoccupation scale. 1) was recalled by the parents, 2) was assessed by a psychologist or doctor, 3) was the subject's description, 4) the parents' retrospective assessment of the subject at 3 to 5 years of age, and 5) was the subject's retrospective assessment of his/her condition at Junior High School. 4) rates social anxiety, general anxiety, separation anxiety and specific phobia and 5) describes self-preoccupation and external preoccupation.

**Results**: Average age at definite diagnosis was 24.7 years in the Delay Group and 14.4 in the Early Group, significantly different. There was no significant inter-group difference in difficulty in child-raising before school age. The PARS peak symptom scale for preschoolers was significantly different (Delay Group 14.1, Early Group 30.0) as was the adolescents/adults scale (Delay Group 19.4, Early Group 25.8). The four social items in preschoolers PARS were marked in both groups, with no inter-group difference. These items may provide a means of earlier diagnosis of the Delay Group. The only significant intergroup difference for the early childhood anxiety scale was for social anxiety (Delay Group 31.7, Early Group 36.8). However the social anxiety score of the Delay Group was higher than the average for preschoolers overall (Nishizawa, 2011). The only significantly different preoccupation was external preoccupation (Delay Group 33.3, Early Group 29.9). All ASD group members showed higher values than average university students for self-preoccupation (37.5) and external preoccupation (27.5) (Sakamoto; 1998).

**Conclusions:** The ASD characteristics of the Delay Group were less noticeable than those of the Early Group. However, (1) social interaction during infancy was somewhat problematical, (2) social anxiety during early childhood was greater than average children, and (3) external preoccupation during Junior High School years were also marked. These may be early signs for the Delay Group.

**137.002 2** The Life of Adults with ASD in Japan: Are They Having a Happy Adulthood?. M. Tsujii*[1], W. Noda[2], T. Hagiwara[3], K. Suzuki[4] and S. Higo[5], (1)*Chukyo University*, (2)*Research Center for Child Mental Development, Hamamatsu University School of Medicine*, (3)*Hokkaido University of Education, Asahikawa*, (4)*Hamamatsu University School of Medicine*, (5)*Kagoshima University*

Background: Since the Act on Support for Persons with Developmental Disabilities has been in effect in 2004, services for children and youth with ASD has gradually increased in Japan. Services for adults with ASD, however, have remained in preparation status. There is a number of issues against supporting independent life of those population including immature adaptive skills for self-independence, perseveration affecting doing household chores, and none or limited leisure skills. Few literature and research in this area are available and practical solutions have not been proposed.

Objectives: The primary focus of the present study was to understand the current status of daily living in adults with ASD in Japan. Specifically, the study analyzed their thoughts for their own life and support needs. Factors related to their independent living, including mental health conditions, community supports, residential issues, were also investigated.

Methods: Sixty-four adults aged 18 to 52 (46 male, 18 female) participated in this study. A set of survey forms was distributed to each participant to fill out. Some participants needed help to understand meanings of the questions. The set was consisted of a questionnaire, the K10 (Furukawa et al., 2003), and the PRIME Screen-Revised (Kobayashi et al., 2008). A questionnaire was developed for the study to survey the participants' current daily living, ideal lifestyle, and mental/medical conditions.

Results: Collected data revealed that more than half of the participants did not have jobs and enough income or savings to keep living by themselves. More than 60 % of the participants reported they were living with their families. Over 70% of them wanted to stay with their families in the future. To the questions regarding the life after their parents' death, although nearly half of the participants told their wish of independent living, they had concerns for living by themselves and needed supports to do so. From the data related to the mental health conditions, results of the K10 indicated that 35.6% of the participants scored higher than the cut-off score, indicating possibilities of having mood/anxiety disorders. Additionally, results of the PRIME-Screen Revised revealed that 20.3% of participants were assessed as "positive" about having prodromal symptoms of psychosis. 14.1% of the participants scored higher than the cut-off score of the K10 and rated "positive" in the PRIME-Screen Revised.

Conclusions: The results indicated that Japanese adults with ASD have a number of concerns and needs for community living. Many of them want to have an independent life; however, they also realize numerous difficulties and the needs of supports. Levels of intellectual functioning and education would not alleviate such problems in the cases of ASD. Additionally, mental health condition could be an another concern. Many of these populations may need to deal not only with their own ASD specific traits, but also with other mental health conditions in their adulthood. The issues regarding availability of community-based services for adults with ASD should be examined thoroughly and resolved immediately to assure their quality of life.

**137.003 3** A Video Self-Modeling Intervention for Postsecondary Students with Autism Spectrum Disorders. N. P. Pierce*[1], T. Falcomata[2], C. Fragale[2], S. Kang[2], S. Gainey[3], D. Longino[2], C. Muething[2], I. Jones[2], J. Aguilar[2] and J. Shubert[2], (1)*The University of North Carolina at Chapel Hill*, (2)*University of Texas at Austin*, (3)*Behavior Solutions*

**Background:** Colleges and universities have experienced a steady growth in student enrollment populations that have included individuals with disabilities (Paul, 2000). Included in the increasing trend of postsecondary students with disabilities are students diagnosed with autism spectrum disorder (ASD). Although academically eligible, research show that students with ASD experience social difficulties in postsecondary settings (MacLeod & Green, 2009). Some research suggests that students with ASD

frequently face social obstacles on campus in several areas including the student union, the student pub, libraries, and student living spaces (e.g., dormitories; Mandriaga, 2010). Mandriaga suggests that these social spaces present difficulties for students with ASD because of their repeated contact with large volumes of students and the difficulty of students with ASD in adjusting to a variety of social settings. Moreover, most universities are unable to provide accommodations that meet the unique needs of individuals with ASD (Smith, 2007). A well-established intervention in addressing social skill development is video-self modeling (VSM). Until now, VSM research has focused on primary and secondary students and not yet investigated the topic of utilizing a VSM intervention for training social skills for individuals in the postsecondary setting. This study assessed the feasibility of using a VSM intervention to improve the social skills of college students diagnosed with ASD. Implications for students with ASD entering postsecondary education, as well as the field of autism spectrum disorders (ASD) are discussed. Further recommendations for future research using VSM technology is provided.

**Objectives:** To determine the efficacy of a VSM intervention for teaching social skills for individuals with ASD in a postsecondary setting.

**Methods:** In this study, a multiple baseline (Kennedy, 2005) across therapists (study 1 and 2) and across participants (study 3) was used to evaluate the effect of a VSM intervention on social skills. Baseline social skills consisted of breaking eye contact (i.e., looking downward and away from the eyes), not initiating conversation with others, and excessive talking during social conversations (i.e., inability to conduct two-way conversation). VSM intervention sessions consisted of participant viewing a video model of themselves demonstrating (targeted) appropriate social skills.

**Results:** Two participants demonstrated an immediate effect in target social behavior, while one showed moderate increases. The final participant showed sizeable increases once the prompt component was added to VSM. Modifications to the VSM procedure (i.e., adding a prompt component) appeared to improve the effectiveness of the intervention on targeted social skills for three of the four students diagnosed with ASD.

**Conclusions:** The results of this study signify a positive effect on social skill behaviors when VSM was introduced for all four participants. Each participant demonstrated increased social skills utilizing VSM to address multiple behaviors while demonstrating considerable flexibility in its implementation (i.e., VSM alone or VSM with prompt). These findings extend the current literature on VSM provided for young children to older individuals diagnosed with ASD who attend college.

**137.004 4** Executive Function in College Students on the Autism Spectrum. S. M. Ryan*, S. Eldred, H. Noble, A. B. Barber and A. T. Gilpin, *University of Alabama*

Background:

Little is known about the characteristics of students with an ASD entering college or what factors significantly impact their transition. Of particular interest are executive function (EF) skills, which have been shown to be impaired in children and adolescents with an ASD (Hill, 2004). Specifically, previous studies show that as children with ASD age, EF improves overall, but worsens compared to same age peers (Rosenthal et al., 2013).

Objectives:

The purpose of the current project is to: 1.) Establish a database for the long-term study of social, emotional, behavioral, academic, and EF outcomes in individuals with HFA at a major public university; 2.) Examine the characteristics of a sample of students with an ASD diagnosis who are entering college, focusing primarily on EF skills, for the purpose of documenting strengths and weaknesses that may impact the college transition.

Methods:

The current study includes 5 students from a college transition and support program for degree-seeking students with an ASD diagnosis at a major public university. As part of the program, students meet 2-3 times per week with a therapist-mentor, attend 4 hours of study hall, and participate in regular group meetings. Each student is administered a battery of measures at summer orientation and toward the end of each

Fall and Spring semesters during their college career. The battery of measures includes parent-report measures (i.e., the BRIEF, SRS, and a daily living skills measure developed by the program), self-report measures (i.e., the BASC-2, STAI, BDI-II, SRS, Brief Multidimensional Life Satisfaction Measure, and the Student Adjustment to College Questionnaire), information provided as part of the application process (i.e., previous testing, high school/community college GPA), and current GPA.

Results:

Preliminary analyses completed on the first cohort entering college in 2012 (n = 5) indicated a mean Full Scale IQ of 118. SRS scores confirm significant social difficulty (mean total SRS score = 74.75). Overall, students reported at-risk levels of difficulty in the areas of Atypicality (mean T-score=61.80) and Hyperactivity (mean=61.80), as well as at-risk levels of concern regarding self-reliance (mean=35.60). The results of the BRIEF indicated significant difficulty in the areas of metacognition and behavior regulation ( mean T-scores : 63.8 and 64.6, respectively). Specifically, the greatest difficulty appeared on the shift subscale (mean=66.4), the initiate subscale (mean=71), and the plan/organize subscale (mean=64.8). Data for an additional 3-5 students will be added over the next few months. Correlations on the larger sample will be used to examine what, if any, impact EF has on social skills, anxiety, and academic performance.

Conclusions:

Overall, these results highlight the unique difficulties faced by students with HFA on a college campus. Despite above average intelligence these students experience significant social and EF difficulty relative to the general population. These difficulties are most apparent in the areas of task initiation, organization, and shifting attention, all of which can cause significant difficulty in the absence of the structure of the home and high school environments. The exact nature of this relationship will be the subject of future longitudinal analysis.

**137.005 5** Growing up with Autism: Effectiveness of a Residential Farm Community Treatment in a Cohort of Adults with Low Functioning Autism. P. Politi*, P. Orsi, M. Besozzi, N. Brondino, U. Provenzani, M. Rocchetti, T. Veglia, M. Boso and F. Barale, *University of Pavia*

Background: autism spectrum disorders (ASDs) are generally regarded as lifelong conditions, although, growing up, individuals with ASDs may show an improvement in different functional and social areas (i.e., behavioral problems, life skills) as well as a reduction in autistic symptoms (i.e., communication and social deficits). Literature data suggest that up to 15–30% of adults with autism will show positive outcomes. Unfortunately, few data are available on clinical outcomes in adults with low functioning autism. This particular group may benefit from residential treatment, provided in particular by farm or agricultural communities, which could represent a lifespan option for these individuals. In fact, animal husbandry as well as horticulture provide a range of different activities which are, however, stable and predictable and thus suitable for patients with autism. Additionally, the rural environment represent an ideal setting for autistic patients in contrast with urban realities: it is noiseless, less crowded and stressful. Cascina Rossago is a Italian farm community for adults with low functioning autism founded in 2002. It comprehend 45 acres of farmland and is home to alpaca and other animals. Cascina Rossago houses 24 permanent residents, which are involved not only in agriculture and livestocking but also participate in carpentry, pottery and textile workshops.

Objectives: the present follow-up study aimed to evaluate clinical changes in a sample of adults with low functioning autism in a residential farm community setting.

Methods: participants were 24 young adults who had received a clinical diagnosis of low functioning autism by a senior psychiatrist. The Leiter International Performance Scale was used to measure intelligence. The Vineland Adaptive Behavior Scales (VABS) were used to assess clinical changes in adaptative domains at admission and at follow-up. The VABS is organized within a four domain structure: Communication, Daily Living Skills, Socialization, Motor Skills. Additionally, all subjects were evaluated with the Autism Behaviour Checklist (ABC), the Childhood Autism Rating Scale (CARS), the Adaptive Behaviour Scale (ABS) and the Diagnostic Assessment for the Severely Handicapped (DASH).

Results: all patients experienced improvement in symptoms and there was a significant increase in all VABS domain ($p<0.05$).

Conclusions: farm communities may be an ideal option for people with low functioning autism. These settings seems to foster clinical improvement in this patient group.

**137.006 6** Intact within-Modal and Cross-Modal Integration of Low-Level Sensory Features in Autism Spectrum Disorder. G. Charbonneau*[1], A. Bertone[2], M. Véronneau[1], S. Girard[1], L. Mottron, M.D.[3], F. Lepore[1] and O. Collignon[4], (1)*Centre de Recherche en Neuropsychologie et Cognition (CERNEC), Université de Montréal*, (2)*Perceptual Neuroscience Laboratory for Autism and Development (PNLab)*, (3)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (4)*Center for Mind/Brain Sciences, University of Trento*

Background:

The brain's ability to integrate information coming from single or multiple sensory modalities is critical for perceiving the world as a unified and coherent percept. These processes, referred to as within-modal and cross-modal integration, ultimately allows us to interact with our surrounding and others in an adaptive manner. We recently demonstrated that individuals with autism spectrum disorder (ASD) do not benefit from the presence of a facilitatory temporally relevant tone during a demanding visual search task (Collignon et al., 2012), and display a reduced ability to integrate visual and auditory representations of the emotional expressions (Charbonneau et al., 2013), suggestive of a decreased multisensory gain in this population. However, controversy remains about multisensory integration in ASD, as alterations in this process were mainly observed for more complex tasks and stimuli (e.g., top-down control; linguistic or social stimuli), with putatively intact ability to integrate simple low-level information (de Boer-Schellekens, Keetels, Eussen, & Vroomen, 2013). Regarding the comparison between multisensory and unisensory integration, we know that redundancy gain (RG), which correspond to the behavioral outcomes of sensory integration, is greater for cross-modal than for within-modal targets in typically developing individuals (TD) (Girard et al., 2013). However, a direct comparison between within- and cross-modal integration has not been investigated in individuals with ASD.

Objectives:

The current study was designed to explore if the alteration in multisensory integration in ASD, as obtained from our previous experiments, can be generalised to within-modal and cross-modal integration of low-level non-social stimuli.

Methods:

Twelve individuals diagnosed with ASD and 12 individuals in a typically developing comparison group, matched for full-scale IQ, were asked to respond as fast as possible to (1) lateralized visual or tactile targets presented alone, (2) double stimulation within the same modality (within-modal condition) or (3) double stimulation across modalities (cross-modal condition). Each combination was either delivered within the same hemi-space (spatially aligned) or in different hemi-spaces (spatially misaligned).

Results:

In contrast with previous reports, no difference was found between ASD and TD in their ability to integrate low level visual, tactile and visuo-tactile stimuli. In both groups, the multisensory gains obtained from the cross-modal conditions were greater than those obtained from combination of two visual or two tactile targets.

Conclusions:

These results clearly demonstrate that individuals with ASD integrate low-level visual and tactile information as efficiently as TD individuals. Moreover, redundancy gain in ASD was found to be greater for cross-modal targets than for within-modal stimuli, extending for the first time to ASD the notion that estimates of the same event that are more independent produce enhanced integrative gains. Overall, these findings suggest that multisensory integration alterations that were previously reported in ASD are probably contingent of the type of information being integrated and/or the paradigm used, and could be restricted to more complex tasks involving either socially-laden information, or top-down processes during sensory integration.

**137.007 7** Longtitudinal Outcomes of Adults with Autism. J. ". A. Odom*[1], L. A. Ruble[1], T. Belkin[2] and J. H. McGrew[2], (1)*University of Kentucky*, (2)*IUPUI*

Longitudinal Outcomes of Adults with Autism

Odom, Ruble, McGrew, & Belkin

Background: Little is known about the lives of adults with autism and their parents. A 20-year follow-up longitudinal study is presented. Several outcomes were evaluated including adaptive behavior, medical issues, employment information, residential status, community inclusion, and self-direction. Parent outcomes such as caregiver burden and concerns for the future for their adult child with autism were also identified.

Objectives: To describe thelongitudinal outcomes of adults with autism and their caregivers.

Methods: A total of 16 parents/caregivers ($M_{age}$= 71; 34% of original sample; Ruble & Dalrymple, 1996) were located and agreed to participate; respondents were 12 mothers, two fathers, and two nonrelated caregivers from a Midwestern state. Most of the caregivers (62.5%) were married, and their spouse was also the parent of the adult with autism; three were widowed. The adults with autism were 14 males and 2 females ($M_{age}$= 42); 15 were White and one was Asian. Caregivers completed the Vineland Adaptive Behavior Scales and an adapted version of the National Core Indicators survey.

Results: Adaptive behavior mean scores were low for the adults (M = 27.9; SD = 14.5). Fifty-six percent received 24-hour supervision and 44% lived with their family. A minority shared a house (n = 38%) or lived in a group home (19%). Fifty-six percent lived in a residence financed by their family. The majority (75%) lived in their current home for more than 5 years. Individuals with autism were reported to be in fair (44%) to excellent (56%) health; however 63% had other medical conditions, including 31% who had seizures. Half of the adults were taking medications for behavior, anxiety, or depression. For services, the majority (69%) were receiving case management. Forty-three percent of the sample required supports for self-injurious or disruptive behavior.Twenty-five percent of parents reported a need for additional services. Only one family was receiving respite care. One adult with autism was competitively employed. Most outings (63%) involved family. They also went out for entertainment (73%) and to a restaurant (100%). All had siblings and 88% of individuals stayed in contact with siblings.

For parents, one-third reported missing work or neglecting other duties due to the care of their child. Thirty-eight percent reported mental and physical health effects and financial strain. Fifty-seven percent reported feeling sad or unhappy; and 50% reported feeling socially isolated. The chief concerns were worry about their child's future (88%), followed by concern for their child's living situation (81%) and availability of future services (75%).

Conclusions: These data describe the outcomes of adults who are nearing middle age. All are involved in community activities and in satisfactory health. Most surprising was that the majority of adults lived at home with their parents and family who provided financing for their housing. Effects on parents will continue as they ageand approach retirement or face declining health, with the most common concern beingproviding for the future for their adult child with autism.

**137.008 8** Adult Daily Routines: A Mixed-Method Approach to Making Meaning. T. C. Daley*[1], N. Singhal[2], T. Weisner[3], R. S. Brezis[3] and M. Barua[2], (1)*Westat*, (2)*Action For Autism*, (3)*UCLA*

Background:

ASD research is increasingly conducted throughout the world, but most of the focus remains on children. This is similarly true in India, where services and other opportunities for adults are extremely limited even in urban areas. How do adults with ASD spend their time? Where are they, who are they with, and what are they doing all day? Does this differ by level of functioning? What causes stress for parents? And what would be most helpful to parents and adults now? These questions can be bundled into what researchers have often called "daily routines" and what has been articulated over the past twenty years as the basis of ecocultural theory (Gallimore, Weisner, Kaufman, & Bernheimer, 1989).

Objectives:

This paper presents data on adult daily routines from a collaborative and mixed-methods project on families of adults with ASD in India.

Methods:

Interviews with parents and adults, observations in the home, direct assessments, and

questionnaires were completed with 52 families of adults (54 adults) with ASD in New Delhi and the National Capital Region. To obtain detailed information about daily routines, parents reported on a typical weekday. These data were transformed into six variables (hours awake/asleep; napping; outside the home; in a structured setting; inside the home in a private space; and spent with different individuals). Transcripts were used to code activities that adults were reported to engage in (e.g., watching TV, going for a walk, reading). Parents completed questionnaires on stress, parent competence and empowerment.

Results:

Higher functioning adults are more likely to have a structured setting and spend time outside the home; adults who stay home do so both because of their preferences and their disruptive behaviors. Adults at home spend an average of 22 hours a day inside. When adults are home, regardless of their level of functioning, they generally spend approximately 75% of their waking time in shared family spaces but during about 60% of this time, they are not interacting with others. Parents report there are not enough suitable work and training centers that are easily accessible. Approximately 70% of both mothers and fathers in this study had levels of stress that are considered in the clinical range; higher parental stress was found in families where mothers worked outside the home but there was no association between parent stress and adult daily routines.

Conclusions:

Most families of adults with ASD have adapted their lives to fit their adults' needs. Still, significant barriers exist for families to access appropriate services for adults in urban India and parents report a range of needs related to their adults. This project used a mixed-methods and community-based participatory research model to understand the daily activities of adults and reasons for these routines. The approach in this study is one that the research community may find of value, as an increasing number of studies focus on adult populations and seek to understand how to better serve adults and their caregivers.

**137.009 9** Role of Parental Occupation in Autism Spectrum Disorder Diagnosis and Severity. A. S. Dickerson*[1], D. A. Pearson[2], K. A. Loveland[3], M. H. Rahbar[1] and P. A. Filipek[1], (1)*University of Texas Health Science Center at Houston*, (2)*University of Texas Medical School, Houston*, (3)*University of Texas Medical School*

Background: Although the specific genotypic aspects of autism spectrum disorder (ASD) have yet to be identified, some investigators have suggested that parents of children with ASD may present with less recognizable autistic-like phenotypic characteristics. Others have suggested that many professionals with highly systemizing occupations are functioning with undiagnosed Asperger's Disorders. However, results from studies on ASD diagnosis and technical occupations of parents have been conflicting.

Objectives: To (1) test associations between reported parental occupations and ASD diagnosis and (2) test the association of parental occupational characteristics on ASD severity in a subsample containing only children with an ASD diagnosis.

Methods: This is a secondary exploratory analysis of data from two previous studies conducted in a sample of 273 children ages 7 to 18 years. The first study was a case-control study of developmental impairment of the orbitofrontal-limbic circuit as a possible biomarker for ASD. The second study was a project designed to assess the behavioral and cognitive aspects of attention deficit hyperactivity disorder (ADHD) in children with ASD. Children for both studies were recruited from the same educational, clinical, and community sources. Suspected ASD cases were determined by clinical interview and observation. Those meeting DSM-IV-TR criteria were administered both the Autism Diagnostic Interview, Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS) to confirm diagnosis. Parental occupations were established through demographic questionnaires during assessment. We used the Standard Occupational Classification (SOC) system to classify occupational characteristics of interest and National Institute of Occupational Safety and Health (NIOSH) reports to determine risk of occupational exposures. We performed logistic regression to explore associations of ASD status with certain white-collar occupations and occupational characteristics and Generalized Linear Models (GLM) to investigate differences in

mean ADOS and ADI-R domain and total scores for parental occupation characteristics.

Results: Demographic characteristics of cases and controls were similar. Fathers of cases were six times more likely to work in healthcare (AOR=6.38, $P<0.01$) and four times more likely to work in finance (AOR=4.60, $P=0.03$) after adjustment for demographic variables. In subanalysis, the mean communication score ($P<0.01$) and social impairment score ($P=0.04$) were higher for children with both parents having technical occupations. Furthermore, in multivariate analysis, mean ADI-R total scores were higher for children of fathers with technical occupations ($P=0.02$). Significance was also seen with higher ADI-R scores for children with both parents having technical occupations ($P=0.03$).

Conclusions: Our findings suggest that there is a joint association between parental occupation and ASD severity, as well as a relationship between paternal occupation and ASD diagnosis. These results are supportive of a "broader phenotype" in parents of children with ASD and assortative mating in adults with these autistic-like characteristics. This effect could be due to genetic or epigenetic predisposition which might contribute to having offspring with greater ASD severity. Therefore, more analysis should be done to determine what factors contribute to occupation choices, and how these factors, if identifiable, can add to the risk of communication or social impairment in the offspring of these individuals.

**137.010 10** The Situation of Adolescents and Adults with Autism and Other Developmental Disabilities in Mainland China. C. Wang*[1] and M. M. Hussey[2], (1)*Nankai University*, (2)*Beijing Normal University*

Background: The first case of autism in China was identified in 1982. Since then, much progress has been made and the first generations of children to be diagnosed are now adults. This population of autistic adults continues to grow as increasing awareness has led to higher rates of diagnosis and presents a new set of challenges for Chinese society on a national level.

Objectives: The objective of the study is to describe the situation of adolescents and adults with autism and other developmental disabilities in China.

Methods: The method used to conduct this research was a sample survey of parents and caregivers of adolescents and adults with autism and other developmental disabilities in Mainland China and follow-up interviews. Questions focused on three major aspects of their lives: access to education/rehabilitation therapy, access to vocational programs/employment opportunities, and impact on the family.

Results: The majority of the adolescents and adults with autism and other developmental disabilities had been denied access to education as children, and this had a major effect on their options in the future. There is also severe lack of employment opportunities, with over 80% of the adults are unemployed and nearly half of the parents' expressing doubts that their child could develop work-related skills. The two commonly expressed concerns were fear that the parents would get sick and not have anyone to care for the child with autism, as well as lack of support from society.

Conclusions: Strategies to improve the situation must begin by addressing the structural problems within the Chinese autism and other developmental disabilities services and special education programs.

**137.011 11** The Use of a Positive Reframing Intervention during Social Conversation in Adults with ASD. A. Navab*, K. Ashbaugh, J. L. Bradshaw, A. R. Miller, T. W. Vernon, T. Gagliardi, N. Okada, L. K. Koegel and R. L. Koegel, *University of California Santa Barbara*

**Background:**

Recent research has indicated that adults with autism spectrum disorders (ASD) are frequently diagnosed with comorbid anxiety and depression disorders (Ryden & Bejerot, 2008; Clarke et al., 2009), as well as higher levels of negative emotions and difficulty with emotion regulation (Samson et al., 2012; Kasari & Sigman, 1997). Furthermore, many adults with ASD have difficulty in social interactions, romantic relationships, and employment (Howlin, 2000). It may be proposed that increased levels of expressed negativity may create difficulties in social conversation, having detrimental ramifications on the development of social friendships, romantic relationships, and ability to acquire and maintain employment.

Positive reframing, or changing one's conceptual and emotional viewpoint in relation to how situation is experienced (Watzlawick, Weakland, & Fisch, 1974), has been empirically validated as a beneficial treatment for a range of psychological conditions, including depression (Lambert, 2010), anxiety (Goldin et al., 2012), PTSD (Moore et al., 2010), and depression and anxiety in parents of children with ASD (Benson, 2010). However, the effectiveness of a positive reframing intervention implemented with adults with ASD has yet to be investigated.

**Objectives:**

The current study investigated the use of a positive reframing intervention in decreasing negative comments during social conversation in adults with ASD. Additionally, global ratings of affect and self-report measures of depression, anxiety, and hopelessness were analyzed before and after implementation of intervention.

**Methods:**

Five adults aged 21-37 diagnosed with ASD participated in this study. Prior to intervention, each participant was receiving occupational intervention not addressing excessive negative comments to conversational partners. A multiple baseline design was employed to evaluate the use of a combination treatment package consisting of self-management and systematic video feedback. During assessment and intervention phases, each participant participated in weekly naturalistic conversational probes. These interactions were videotaped and coded for negative comments and affect. Additionally, self-report measures of depression and anxiety including the Beck Depression Inventory-II (BDI-II), the Beck Hopelessness Scale (BHS), and the Beck Anxiety Inventory (BAI) were completed at baseline and every four intervention sessions to assess for general emotional functioning.

**Results:**

Results indicated that despite continuing vocational interventions, all participants engaged in negative commenting and experienced persistent symptoms of depression and anxiety during the baseline phase. Following the positive reframing intervention, all participants exhibited decreased negative commenting and increased positive affect during social conversation. Furthermore, decreases in depression, anxiety, and hopelessness were indicated by the BDI-II, BAI, and the BHS. High levels of inter-observer agreement were found between video coders, as well as high Kappa coefficients.

**Conclusions:**

The present study provides preliminary evidence that a positive reframing intervention may be effective for improving adults' social interactions with peers. The addition of self-report measures may provide new insight in regard to the potential for such an intervention to improve symptoms of depression and anxiety as well. Furthermore, preliminary data suggests that such an intervention may produce collateral gains in affect. These results have significant implications for improving social interactions, developing friendships, and accessing and maintaining employment.

**137.013 13** Social Support As a Moderator of the Relation Between Sibling Relationship Attitudes and Depressive Symptoms Among Typically-Developing Adult Siblings of Those with Autism Spectrum Disorder. T. S. Tomeny, E. C. Fair* and T. D. Barry, *The University of Southern Mississippi*

Background: Literature examining typically-developing (TD) siblings of individuals with autism spectrum disorder (ASD) remains inconclusive. Some studies suggest siblings may experience maladjustment, others suggest possible benefits, whereas others have found no differences in overall development (Meadan et al., 2010). Thus, it has been suggested that future research should focus on identifying specific risk and protective factors for TD sibling adjustment. Early sibling interactions and attitudes are thought to have potentially longstanding influences on behavior and development across the lifespan (Cicirelli, 1995; Riggio, 2000). Perceptions of high levels of social support have also been found to act as a buffer against stressors, protecting individuals from negative outcomes (Armstrong et al., 2005). Because TD adult siblings often eventually take over care of their siblings with ASD (Orsmond & Seltzer, 2007), examination of factors related to TD sibling well-being warrants consideration.

Objectives: The purpose of the current study was to examine perceptions of social support as a potential protective factor against depressive symptoms among TD adult siblings of those with ASD. It was predicted that perceptions of social support would moderate the relation between child and adult attitudes about the sibling relationship and depressive symptoms.

Methods: Fifty-three typically-developing adult siblings [ages 18-68 (*M* = 30.58, *SD* = 13.7); 85% female] of individuals with an ASD participated. Siblings completed a demographic form, the Interpersonal Support Evaluation List (ISEL) to assess perceived overall social support, the Lifespan Sibling Relationship Scale (LSRS; Riggio, 2000) to assess child and adult attitudes about the sibling relationship, and the Depression Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995) to assess current depressive, anxious, and stress symptoms.

Results: Two separate moderated multiple regression analyses were conducted with sibling gender, age, income, and childhood family size entered in Step 1 as controls. After centering the scores, the predictor variables and moderator variables were entered in Step 2. The interaction terms were entered in Step 3. Results of the first analysis revealed a significant interaction between TD sibling perceptions of social support and TD sibling child relationship attitudes when predicting depressive symptoms in TD siblings, $\Delta F(1, 45) = 9.19$, $p = .004$, $\Delta R^2 = .088$. Results of the second analysis revealed a significant interaction between TD sibling perceptions of social support and TD sibling adult relationship attitudes when predicting depressive symptoms in TD siblings $\Delta F(1, 45) = 4.44$, $p = .041$, $\Delta R^2 = .045$. As expected, interaction plots of both analyses showed that TD siblings who exhibited more negative child and/or adult sibling relationship attitudes and lower levels of perceived social support were more likely to have higher levels of depressive symptoms.

Conclusions: As predicted, perceptions of social support moderated the relations between child and adult sibling relationship attitudes and depressive symptoms among TD adult siblings of those with an ASD after controlling for sibling age, gender, income, and childhood family size. Overall, these results suggest that those siblings with negative attitudes about their sibling relationship and low levels of perceived social support may be at greater risk for depressive symptoms.

**137.014 14** The Role of Perceived Teacher Autonomy Support in Promoting Postsecondary Education Expectations in Students with Autism Spectrum Disorder. E. A. Klinepeter*, W. McWherter, S. Mazur, C. G. Connolly, C. M. Gatto and J. J. Diehl, *University of Notre Dame*

Background: Both students with autism spectrum disorder (ASD) and peers with a non-ASD intellectual disability are at risk for poor postsecondary outcomes. Participation in postsecondary education has the potential to improve outcomes and overall standard of life; however, lack of participation in these settings and low expectations of success remain pressing issues. Self-determination can play an important role in promoting transition outcomes among students receiving special education services, yet little research has examined how to promote these skills among students with ASD. Teacher autonomy support has been identified as one means by which to promote self-determination and, in turn, school-related outcomes among typically-developing students. Thus, there is reason to believe teacher autonomy support can play an important role in promoting self-determination and postsecondary education expectations of students with ASD and their peers.

Objectives: The purpose of this study was: 1) to examine the role of perceived teacher autonomy support in postsecondary education expectations of students with ASD and non-ASD intellectual disability, as mediated by self-determination; and 2) to compare student vs. parent reports of expected postsecondary education attendance, success, and transition planning inclusion.

Methods: Preliminary results include 12 individuals with ASD and 5 individuals with intellectual disability between the ages of 16-21 years. All had a primary diagnosis of ASD or intellectual disability listed on their IEP and had formally begun transition planning. Diagnoses were independently confirmed using the Social Communication Questionnaire-Lifetime for students with ASD and the Wechsler Abbreviated Scale of Intelligence-Second Edition for individuals with intellectual disability. Participants were administered three questionnaires related to perceived teacher autonomy support, self-determination, and postsecondary education

expectations and transition planning. Parents also completed the final questionnaire.

Results: Using bootstrap regression analyses, preliminary data suggest that perceived teacher autonomy support is significantly related to students' expectations of postsecondary education attendance, 95% CI [0.48, 198.60], and success, 95% CI [0.44, 295.45]. Self-determination partially mediated the relationship between perceived teacher autonomy support and students' expectations of postsecondary education attendance, 95% CI [0.20, 100.33], although not success, 95% CI [-23.62, 253.88]. Additionally, parents more often reported students were included in transition planning, $X^2(1, N=17) = 4.50$, $p<0.05$. Parents also showed a trend toward reporting more positive expectations of postsecondary education attendance than students, $X^2(1, N=17) = 3.36$, $p<0.10$, although reported expectations of success did not significantly differ.

Conclusions: Overall, we found that perceived teacher autonomy support is an important factor in promoting positive expectations of postsecondary education attendance and success among students with ASD or intellectual disability, and self-determination may play a role in this relationship. Additionally, students are often unaware of their role in transition planning and the possibility of postsecondary education. This study highlights the importance of targeting teacher autonomy support in classrooms and lays the groundwork for future studies that examine this vastly understudied topic - ways to promote positive postsecondary outcomes for students with an intellectual disability or ASD while still in high school. Future studies should more fully examine school practices that lead to optimal postsecondary outcomes among students.

**137.015 15** Informed Consent in Adults with Autism: Ethical and Legal Considerations in the United States. B. A. Jerskey*[1], E. D. Correira[2] and E. M. Morrow[3], (1)*Alpert Medical School of Brown University/Bradley Hospital*, (2)*Correira & Correira LLP*, (3)*Brown University*

Background: The process of obtaining informed consent is guided by many ethical values such as autonomy, beneficence, and justice. At times these principles are in conflict, directing researchers to seek guidance at the institutional, state and federal level. When it comes to consenting individuals who may lack the capacity to make a truly informed decision about participation, a disparity arises between autonomy (the ability for a person to make their own decisions) and justice (the fair selection of research participants). Historically protections have been put in place to shield potentially vulnerable populations including children, prisoners, pregnant woman and individuals who may have reduced capacity to consent. The protections set in place for these groups were patriarchal in nature, in that, these groups were thought to be at greater risk for exploitation and misuses. However, this protection has lead to the restriction of participation in research in turn diminishing the evidence-base for vulnerable populations.

Objectives: A large proportion of adults with autism have intellectual disability and/or are non-verbal making it difficult to assess their capacity, and thus challenging to obtain informed consent. The current investigation aims to evaluate the matter of informed consent with regard to these low-functioning adult individuals with autism.

Methods: We conducted a search in Lexis Nexis for legal and news related articles, Casemaker for case law and statutes, and PubMed for relevant scientific articles in policies and practice with intellectual disability/capacity to consent.

Results: Our investigation of the law and scientific literature revealed that federal regulations are silent on who can act as a legally authorized representative for adults with autism regarding participating in research. This leaves the onus at the state level. Six states in the US have enacted surrogate consent statutes for research, however, all but one limit the surrogate's authority. When no laws exist, it is often the institution that sets the bar in regard to safeguards for human subjects; remarkable variability between institutions suggests a need to create a "common practice." Our research investigating adults with autism and their transition to adulthood has found that approximately 50% of our participants are their own legal guardians for a variety of reasons, not limited to the financial burden associated with seeking guardianship, avoidance of seeking judicial involvement, or lack of a sufficient surrogate.

Conclusions: We recognize that a diagnosis does not define a person's level of capacity, thus when

obtaining consent, we have proposed and currently use a 'consent survey' to assess the perspective participant's understanding of the research and its personal relevance. However, we have yet to develop means of assessing capacity in individuals who are non-verbal; protocols involving surrogate and/or waived consent in certain circumstances are an option for consideration. It is crucial that we allow all individuals to participate in research that is of minimal or minor over minimal risk. Not only are there ethical considerations in denying these participants the potential benefits that research can offer, it is a necessary step toward obtaining knowledge about all adults with autism.

**137.016 16** A Multi-Site Implementation of a Social Skills Training Program (PEERS) to Improve Friendships for Adolescents with Autism Spectrum Disorders. B. Straith*[1], S. Oczak[2], J. Bebko[2], M. Thompson[1], T. MacDonald[1], M. Spoelstra[1], R. Ward[3], S. Duhaime[1], M. Segers[2] and S. Zdjelaric[2], (1)*Autism Ontario*, (2)*York University*, (3)*Brock University*

Background: In general, friendships in adolescents with Autism Spectrum Disorder (ASD) differ in quantity and quality from the friendships of their typically developing peers (Bauminger et al., 2008). There are both practical and clinical implications supporting friendship development in adolescents with ASD, taking into account socio-cognitive characteristics and difficulties related to affect. Exploring the mechanisms that assist friendship development in adolescents with ASD may provide insight into how this population learns and applies social behaviour.

Adolescents with ASD exhibit significant social skill deficits that contribute to academic, behavioural and emotional difficulties. Typically developing adolescents often learn basic social norms by observing others; however, adolescents with ASD often require planned, explicit instruction in order to acquire pro-social behaviours (Gralinski & Kopp, 1993). The UCLA-based Program for the Education and Enrichment of Relational Skills (PEERS; Laugeson, Frankel, Mogil & Dillon, 2008) employs evidence-based practice for the instruction of social skills to adolescents with ASD (Gresham et al., 2001).

Objectives: The present study will explore the mechanisms of friendship development in adolescents with ASD, taking into account ASD symptomatology, social skills knowledge and social anxiety while participating in the PEERS program. To date, two groups have been assessed (n = 16); however, three groups (n = 25) will have completed the PEERS program by December, 2013.

Methods: The present study assesses adolescents with high-functioning ASD between the age of fourteen and seventeen across the province of Ontario, Canada. Over fourteen sessions, adolescents and their parents work with group leaders to learn social skills and behaviours that promote friendship development. Data has been collected from both parent and adolescent groups using a battery of standardized and non-standardized assessments.

Results: Data from two groups (n = 16) indicate that adolescents are initiating significantly more social activities and have improved their social skills knowledge. Supplementary analyses reveal an inverse relationship between ASD symptoms and social anxiety, suggesting that adolescents with fewer ASD symptoms are expressing heightened anxiety ($r$ = - 0.81 < 0.05). This relationship may indicate that adolescents who are aware of their social and communicative deficits are experiencing anxiety during social activities. Finally, a significant relationship between adolescents' friendship qualities and social stress was also found ($r$ = .65 < 0.05), suggesting there is a level of anxiety associated with social interactions.

Conclusions: High-functioning adolescents with ASD are initiating more social gatherings as a result of participating in the PEERS program. There is a level of social anxiety associated with engaging social situations, coinciding with exploring, making and maintaining friendships. It is relevant to address the presence of social anxiety as high-functioning adolescents with ASD attempt to build and maintain meaningful relationships. There are clinical and practical implications supporting the management of social stress in high-functioning adolescents while they form friendships. With increased emphasis on social relationships, adolescent participants may become more comfortable engaging social behaviour; however, additional research is needed to explore this.

## 138 Brain Function

**138.017 17** Cerebral Basis of the Decision-Making Difficulties Experienced By Persons with Autism Spectrum Disorder in an

Unstable Context. S. Robic[1], S. Sonié[1], M. Joffily[2], P. Fonlupt[1], M. A. Hénaff[1], D. Ibarrola[3], G. Coricelli[4], J. Mattout[1] and C. Schmitz*[1], (1)*Lyon Neuroscience Research Center*, (2)*GATE-LSE*, (3)*CERMEP*, (4)*University of Southern California*

**Background:** Constructing an accurate representation of the world, despite its uncertainty, is a challenge for people with autism. These difficulties could be even more obvious in a social environment because of its very changing nature. In a previous study (Robic et al., submitted), we found that an unstable context constitutes a major source of difficulty for people with Autism Spectrum Disorders (ASD) that impacts the decision-making process. A cross effect between the influence of the social nature of the environment and its instability was also found.

**Objectives:** We conducted an fMRI study, aiming at determining the neural correlates of the difficulties experienced by ASD people in an unstable context. We investigated the influence of an environment either stable (associated with constant probabilities) or unstable (associated with changing probabilities), either social or non-social, on the brain activity of persons with High Functioning Autism (HFA) and Asperger Syndrome (AS) compared to controls.

**Methods:** We proposed a lottery task, adapted from Behrens et al. (2008), to sixteen subjects with High-Functioning Autism (HFA) or Asperger Syndrome (AS) and 16 controls matched with respect to age, gender and IQ. Participants were presented with two boxes with hidden reward probabilities and were asked to choose between them. The goal was to score as many points as possible. A cue was presented at the beginning of each trial before the participants made their choice. In the non-social environment the cue was an arrow, in the social one the cue was a movie, which depicted the choice of an actor. Participants received feedback about their choice after each trial and their score updated accordingly. In each kind of environment (social and non-social), two conditions were proposed: a stable (constant probabilities) and an unstable one (probabilities switched every 20 trials). The study was conducted using a 1,5 Tesla MRI scanner. Functional data were analyzed using the SPM8 software package.

**Results:** HFA/AS participants showed lower performance than controls. They also showed a difficulty to redirect their attention when contextual cues were not relevant. We found in HFA/AS participants a weaker engagement of a fronto-parietal attentional network in an unstable context (regardless whether the cue was social or non-social). Importantly, this difference was not observed in the stable context. We found in controls a greater activation of the ACC in the unstable context compared to the stable one, but not in HFA/AS participants. Despite the fact that HFA/AS subjects succeeded in the task in the same proportion than controls in the social environment, social information processing activated regions involved in action understanding and emotion processing to a greater extent in controls than in HFA/AS subjects.

**Conclusions:** We propose that the impaired ability to build prediction in an unstable context experienced by persons with autism could be linked to a less important engagement of both the attentional cerebral network and the ACC, a key structure involved in the estimation of the context instability. This deficit might not be specifically linked to the social nature of the information.

**138.018 18** Decreased Intrinsic Connectivity Between Motion Processing Areas in ASD. J. Suttrup*[1], L. McKay[1], C. Keysers[2] and M. Thioux[1], (1)*Netherlands Institute for Neuroscience*, (2)*UMCG Groningen*

Background: A dysfunction in biological motion processing has been suggested to contribute to social deficits in autism spectrum disorder (ASD). Emerging evidence suggests a specific impairment in orienting towards biological motion. This effect has been repeatedly reported for autistic children and adolescents, however results for autistic adults are more ambiguous. Some neuro-imaging studies focused on the neural correlate of motion detection and a hypo-activation of the posterior superior temporal sulcus (pSTS) was the most consistent finding. However, so far little work has been done on spontaneous, uninstructed biological motion detection and the connectivity between brain regions involved in biological motion processing in ASD.

Objectives: Compare networks for biological motion processing in ASD and control subjects during spontaneous, uninstructed motion detection with a special focus on network connectivity.

Methods: 15 high-functioning autistic adults and 15 controls, matched for age, handedness and IQ participated in this study. Behavioral and functional MRI data were collected during a single MRI scanning session. Three hierarchically ordered conditions were utilized: 1) displays of original point light recordings of human full body motion, 2) displays with homogeneous velocity profiles and 3) displays with homogeneous velocity profile and randomized starting position for each trajectory. Importantly, participants were not instructed to attend to the motion displays but to count the occurrences of a randomly appearing red dot. Standard fMRI pre-processing steps were applied and a group comparison in regional BOLD signal strength was executed using a 2x3 mixed-model ANOVA design. Moreover, a dynamic causal modeling (DCM) analysis was conducted using a linear forward model of the regions MT+ -> EBA -> pSTS -> PF, a driving input to MT+ (conditions: 1+2+3), and modulation effects of shape (conditions: 1+2) and biological motion (condition 1) on the intrinsic connections.

Results: Both groups achieved a high level of performance in detecting the colored dot. The strength of BOLD signal was comparable between both groups in motion processing regions, such as MT+, EBA, pSTS and PF. As a preliminary DCM result, we found a reduced intrinsic connectivity between all the nodes involved in biological motion processing included in our model in the ASD compared to the control group (main effect of group: $F(1,28)=6.7$, $p<0.05$, mixed-design ANOVA). The input effect to the DCM model and the modulation effects of shape and biological motion were significant but did not differ between groups.

Conclusions: In a task that does not require attention to motion, including biological motion, HFA adults recruit the same areas for motion processing as the control participants and show comparable level of BOLD activation. Thus, a strong, automatic processing of motion cues by HFA adults can be concluded. The reduced intrinsic connectivity between the DCM nodes was not specific to biological motion and might indicate reduced baseline connectivity between motion processing areas. The 'red-dot detection' task performance was high in both groups indicating that an influence of this distractor on the connectivity pattern is unlikely. Thus, we propose that the reduced intrinsic connectivity might reflect a neural correlate of motion processing deficits in autism.

**138.019 19** Increased Resting State EEG Gamma Power in Children with HFA. A. Nijhof*[1], R. Raymaekers[2] and J. R. Wiersema[1], (1)*Ghent University*, (2)*Vlaamse Vereniging Autisme*

Background: There is a growing body of evidence indicating that individuals with autism spectrum disorder (ASD) show abnormal patterns of gamma (> 30 Hz) oscillations in their EEG. These abnormalities have been observed during perceptual and cognitive processing but more recently also during resting state conditions. Excessive power in the gamma frequency band has been argued to reflect abnormally high excitability of cortical structures and/or a temporal binding deficit. Resting state EEG studies on gamma power in children with ASD are however still scarce.

Objectives: To investigate resting state EEG gamma power in children with high-functioning autism (HFA).

Methods: A group of children (9 to 13 years) with HFA were compared with a group of age-matched typically developing peers. Eyes-closed resting EEG was measured for three minutes, using a 128-channel EEG system. Power in the gamma frequency band was extracted from the EEG signal and compared between groups.

Results: As hypothesized, children with ASD showed higher power in the gamma band. Importantly, this increase of gamma activity was found at electrode positions that are distant from potential sources of myogenic artefacts.

Conclusions: Excessive resting state EEG gamma power in children with ASD seems to represent a robust phenomenon, which may have important implications for diagnostics and interventions. However future studies are needed to investigate the specificity of the findings by directly comparing clinical groups and to elucidate the functional meaning of enhanced gamma in ASD.

**138.020 20** Metabolite Alterations in Youth with Autism Spectrum Disorder: A Pilot Proton MR Spectroscopy Study. C. D. Jiménez-Espinoza*, *Univesidad de La Laguna. Laboratorio de Neuroquímica y Neuroimagen*

Background:

**Previous studies have investigated different patient populations and $^{1}$H-MRS techniques;**

**it is difficult to draw definitive conclusions regarding the metabolic abnormalities in patients with autism spectrum disorders (ASDs).**

Objectives:

**The purpose of this study was to asses the role of proton magnetic resonance spectroscopy ($^1$H-MRS) in the detection of changes in cerebral metabolite levels in youth autistic.**

Methods:

**This case-control study included 10 right-handed youth (median age, 22 years ± 2.2), and 10 healthy age matched healthy controls (median age, 20.6 years ± 2.2). The diagnosis of autism was established by neurologist, psychiatrist and psychologist in every case. The Autism Spectrum Quotient (AQ), designed by Baron-Cohen et al. to asses Autistic Spectrum traits in intellectually competent adults in both the general population and the Autism Spectrum community. Imaging was performed on a 3.0-T scanner utilizing a single-voxel point-resolved spectroscopy technique. The volume of interest (VOI) was located in the bilateral anterior cingulated, and bilateral posterior cingulated. Peak areas and ratios to creatine (Cr) of N-acetylaspartate (NAA), choline (Cho), and myo-inositol (mI) were analized.**

Results:

**We showed lower N-acetylaspartate/creatine (NAA/Cr), N-acetylaspartate/myoinositol (NAA/mI), Choline/Creatine (Cho/Cr), and myoinositol/Creatine (mI/Cr) in the bilateral anterior cingulated in the study group comparing with healthy controls. The ratio of N-acetylaspartate/creatine (NAA/Cr), N-acetylaspartate/myoinositol (NAA/mI), and Choline/Creatine (Cho/Cr) was increased in youth autistic in the bilateral posterior cingulated, in contrast the ratio myoinositol/Creatine (mI/Cr) was decreased.**

Conclusions:

**$^1$H MRS can provide important information regarding abnormal brain metabolism. Differences in NAA/Cr, NAA/mI, Cho/Cr, and Mi/Cr may contribute to the pathogenesis of autism.**

**138.021 21** Reduced Interhemispheric Functional Connectivity of Children with Autism: Evidence from Functional Near Infrared Spectroscopy Studies. H. Zhu[1], Y. Fan[2], H. Guo[3], D. Huang[2] and S. He*[4], (1)*Centre for Optical & Electromagnetic Research, School of Psychology, South China Normal University*, (2)*Guangzhou Cana School*, (3)*School of Psychology*, (4)*School of Electrical Engineering, Royal Institute of Technology (KTH)*

Background: Autism spectrum disorder (ASD) is a neuro-developmental disorder characterized by abnormalities of neural synchronization.There are growing evidences showing the important role of frontal lobe and temporal lobe in autism brain research. Anatomically, evidence showed increased frontal cortex lobe volume and abnormal temporal gray matter volume. Functionally, abnormal activation and connectivity were found in specific frontal and temporal area of autistic brain. By using fMRI, a few research studies have revealed that ASD is linked to an abnormal pattern of resting-state functional connectivity (RSFC). Reduced interhemispheric correlation in inferior frontal gyrus (IFG) and superior temporal gyrus (STG) emerges very early (12-24 months), which could be an important early diagnostic mark for autism. Functional near infrared spectroscopy (fNIRS) have been previously used for studying autistic patients under certain cognitive tasks. So far there is no report of fNIRS study on the RSFC in autistic children.

Objectives: In this paper we propose to use fNIRS as a cheaper and easy-to-operate neuro-imaging technique to find some characteristic features of RSFC neural activity of autistic children. As inferior frontal cortex (IFC) and temporal cortex (TC) have been shown by many previous studies to be two most relevant cortexes of the autistic brain, we suppose our study would provide more specific hemodynamic response (HbO, Hb and HBT) in these regions. As IFC and TC are very close to each other anatomically, both inter-region, local (between IFC and TC in the same hemisphere) and long-distance (interhemispheric) connectivity could be studied in ASD and typical-developed (TD) children.

Methods: fNIRS is used to study the difference in functional connectivity in left and right inferior

frontal cortices (IFC) and temporal cortices (TC) between autistic and typically developing children between 8-11 years of age. 10 autistic children and 10 typical ones were recruited in our study for 8-min resting state measurement.

Results: The overall interhemispheric correlation of HbO was significantly lower in autistic children than in the controls. In particular, reduced interhemispheric connectivity was found to be most significant in TC area of autism. Autistic children also showed significantly lower local connectivity in right temporal cortex. In correlation maps, autistic children lose the symmetry in the patterns in temporal cortex.

Conclusions: These results suggest the feasibility of using the fNIRS method to assess abnormal functional connectivity of the autistic brain and its potential application in autism diagnosis.

**138.022 22** Source Localization Analyses of Preattentive Auditory Discrimination Processing in Japanese Children with Autism Spectrum Disorders. H. Takahashi*[1], T. Nakahachi[2], S. Komatsu[2], Y. Iida[2], J. Okajima[2], K. Ogino[2] and Y. Kamio[1], (1)*National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*, (2)*National Center of Neurology and Psychiatry.*

Background: Children with autism spectrum disorders (ASD) are often characterized as having atypicalities in information processing deficits, spanning from low level sensory processing to higher-order cognitive functions. Mismatch negativity (MMN) and P3a, which is considered to be promising neurophysiological indexes in translational research of psychiatry, are event related potential (ERP) components that are automatically elicited in response to unattended changes in ongoing, repetitive stimuli. Recent studies suggest that investigation of these preattentive auditory discrimination processing might extend understanding of the atypical neurophysiological basis of ASD. However, to our knowledge, the neural substrates of these atypical responses in ASD are not fully understood.

Objectives: To evaluate the preattentive auditory discrimination processing (MMN and P3a) and their generators in Japanese children with ASD and typical development (TD), and, to evaluate their relationship to quantitative autistic traits.

Methods: In this study, 8 children with ASD and 26 with TD underwent 64 channel EEG testing using a multi-feature auditory oddball paradigm (3 types of deviant: duration, frequency, omission) while passively watching a silent video. We separately average the ERPs in response to the standards and the oddball stimuli, and then subtract the standard responses to get difference waveforms reflecting just the additional processing associated with the oddball stimuli. Based on the electric potential distribution of ERP difference waveform, the exact low resolution brain electromagnetic tomography (eLORETA) software was used to compute the cortical three-dimensional distribution of electric neuronal activity, current density of MMN (latency: 135-205 msec) and P3a (latency: 250-300 msec) components in the subjects as well as the brain regions associated with atypicalities observed among ASD children. ASD characteristics of all subjects were assessed by Social Responsive Scale (SRS).

Results: The current density components of MMN and P3a responses to duration and frequency oddball mapped onto neural sources broadly distributed across temporal, frontal, and parietal regions in children with ASD and TD. Non-parametric voxel-by-voxel regression analysis after logarithmic transformation of the current density data revealed significant negative association between duration-deviant MMN current density of right inferior frontal gyrus and SRS total score. Duration-deviant P3a current density of right inferior, middle, superior frontal gyrus was negatively associated with SRS social cognition subscale.

Conclusions: Our findings support the idea of atypical preattentive auditory discrimination processing in ASD. Further investigations are required to reveal the contribution of the neural sources to atypical higher-order psychosocial cognitive functions in ASD.

**138.023 23** Abnormal PRE-Attentive Arousal and Auditory Sensory Modulation Difficulties in Children with Autism Spectrum Disorders: An ERP Study. T. Stroganova[1], V. Kozunov[2], I. Posikera[1], I. Galuta[2], V. Gratchev[3] and E. Orekhova*[4], (1)*Psychological Institute of Russian Academy of Education*, (2)*Moscow State University of Psychology and Education*, (3)*Mental Health Research Center of Russian Academy of Medical Sciences*, (4)*Moscow State University of Psychology and Education*

**Background:** Auditory sensory modulation difficulties and problems with automatic re-

orienting to sound are well documented in autism spectrum disorders (ASD). Abnormal preattentive arousal processes may contribute to these deficits.

**Objectives:** We investigated in children with ASD the link between 'obligatory' components of the cortical auditory evoked potential (CAEP) reflecting preattentive arousal and auditory sensory modulation difficulties.

**Methods:** Nineteen boys with ASD and nineteen typically developing (TD) boys aged 3-8 years participated in the study. Pairs of clicks ('S1' and 'S2') separated by a 1 sec S1-S2 interstimulus interval (ISI) and much longer (8-10 sec) S1-S1 ISIs were presented monaurally to either the left or right ear.

**Results:** In TD children, the P50, P100 and N1c CAEP components were strongly influenced by temporal novelty of clicks and were much greater in response to the S1 than the S2 click. Irrespective of the stimulation side, the 'tangential' P100 component was rightward lateralized in TD children, whereas the 'radial' N1c component had higher amplitude contralaterally to the stimulated ear. Compared to the TD children, children with ASD demonstrated 1) reduced amplitude of the P100 component under the condition of temporal novelty (S1) and 2) an attenuated P100 repetition suppression effect. The abnormalities were lateralized and depended on the presentation side. They were evident in the case of the left but not the right ear stimulation. The P100 abnormalities in ASD correlated with the degree of developmental delay and with the severity of auditory sensory modulation difficulties observed in early life.

**Conclusions:** The results suggest that some rightward-lateralized brain networks that are crucially important for arousal and attention re-orienting are compromised in children with ASD and that this deficit contributes to sensory modulation difficulties and possibly even other behavioral deficits in ASD.

**138.024 24** Anxiety in Autism Spectrum Disorder Is Associated with Abnormal Prefrontal Cortex Activity. A. McVey*[1], L. Guy[1], C. M. DeLussey[1], J. Worley[1], K. Rump[1], H. Dingfelder[2], C. Chevallier[1], G. Kohls[1], R. T. Schultz[2], J. Miller[1] and J. Herrington[1], (1)*Center for Autism Research, The Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*

**Background:** Autism spectrum disorder (ASD) is often characterized by intense emotional responsiveness and poor emotion regulation. Emotion dysregulation often takes the form of increased anxiety in ASD. While very little is known about the neurobiology of anxiety in ASD, the literature on pediatric anxiety disorders has converged on a model where the emotion functions of subcortical structures (namely amygdala) are poorly regulated by prefrontal cortex (PFC). This model has yet to be robustly tested in samples of individuals with ASD who have co-occurring anxiety disorders.

**Objectives:** The present study tests the hypothesis that co-occurring anxiety disorders in ASD are associated with abnormal PFC activity, amygdala activity, or both.

**Methods:** Data presented here are part of an ongoing study examining the psychophysiology of anxiety and emotion regulation deficits in ASD. To date, 21 participants with ASD have been scanned using a selective attention facial identity task based on that of Vuilleumier and colleagues. The task involves the simultaneous presentation of two pairs of faces and houses. Participants were asked to selectively attend to either the face or house pairs and make a subordinate-level identity judgment. Faces were either neutral or angry. Analyses to date have examined the main effects of selective attention (face versus house judgment) and emotional valence (angry versus neutral faces). All participants met criteria for ASD on a combination of the ADOS, SCQ, a developmental interview (typically the ADI-R), and clinical judgment. Our sample also received in-depth phenotyping for anxiety following the Anxiety Disorders Interview Schedule (ADIS). A total of 11 participants met our study criteria for anxiety (the ASD+Anxiety group, as opposed to ASD Alone). There were no significant differences in age or gender between ASD+Anxiety and ASD Alone groups.

**Results:** Selective attention to faces was associated with decreased dorsal and ventromedial PFC activity in the ASD+Anxiety group (versus ASD Alone). Conversely, perception of angry versus neutral faces was associated with increased ventromedial PFC (anterior cingulate cortex) activity in the ASD+Anxiety group. At the present sample size, no significant difference was identified in

amygdala activation between the ASD+Anxiety and ASD Alone groups.

**Conclusions:** The data from this ongoing study indicate that anxiety in ASD is associated with abnormal PFC activity. Furthermore, the data suggests that this population may be relatively emotionally disengaged to faces, but hypervigilant when presented with emotionally charged faces. This has real-world implications for social and communication development in individuals with both ASD and anxiety.

**138.025 25** Assessing Lateral Interactions within the Early Visual Areas of Adults with Autism. S. Censi*[1], M. Simard[2], L. Mottron, M.D.[3], A. Bertone[3] and D. Saint-Amour[4], (1)*McGill University*, (2)*CHU Sainte-Justine*, (3)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (4)*Université du Québec à Montréal*

Background:

Although atypical performance on visuo-spatial tasks targeting early, non-social perception is a defining characteristic of autism, few biologically plausible hypotheses are available to explain them. Some authors have theorized that persons with autism may have atypical local connectivity resulting in altered response properties of early visual feature detectors (Vandenbrouke et al 2008; Keita et al 2011). One manner to assess such hypotheses is to measure and define local neural activity originating from lateral interactions within early visual areas. This can be done by measuring steady-state visual evoked potentials (ssVEPs) elicited during visual stimulation that specifically targets lateral cortical interactions. One such stimulation is exemplified by the windmill-dartboard paradigm (Ratliff & Zemon, 1982), which consists of a radial pattern comprising concentric contrast reversing zones with contiguous static zones. The varying contrast at the borders of contiguous static and dynamic segments of the windmill-dartboard stimulus result in highly localized lateral interactions (Ratliff & Zemon, V, 1982). In addition, lateral masking paradigms - where low-contrast Gabors are presented either in isolation (target), or flanked by collinear/orthogonal Gabors at different contrasts and target-flanker distances - can also be used measure lateral cortical interactions (Polat et al, 1997).

Objectives:

The objective of this study was to systematically assess lateral interactions between neurons within early visual areas in autism by measuring steady-state visual evoked potentials (ssVEPs) elicited by (i) windmill-dartboard and (2) lateral masking paradigms.

Methods:

Nine participants with autism and 9 typically developing participants, matched for full-scale IQ and age (18-30 years), were asked to passively view visual stimuli during windmill-dartboard and lateral masking paradigms while ssVEPs from four electrodes over the occipital cortex (Oz, POz, O1 and O2) were collected. For the windmill-dartboard paradigm, first- and second-harmonic components of the steady-state responses were used to calculate indices reflecting facilitatory (FI) and inhibitory (SI) cortical interactions for all participants. For lateral masking paradigm, ssVEP data was collected while participants viewed low-contrast Gabor patches presented ether in isolation (target), or flanked by collinear/orthogonal Gabors at different contrasts (8, 16, 30%) at target-flanker distances (1.5λ, 3 λ, 6 λ).

Results:

Group differences were not evidenced for either FI or SI cortical interaction indices obtained during the windmill-dartboard task. For the lateral masking paradigm, an expected difference between collinear and orthogonal Gabors (presented at a contrast of 16%) at target-flanker distances of 1.5 λ was found in the control group, $p = 0.018$. Importantly, this difference was not evidenced for the autism group.

Conclusions:

Our results to date measured using the windmill-dartboard paradigm suggest that facilitatory (FI) and inhibitory (SI) cortical interactions within early visual brain areas are similar in autism and control groups. However, group differences on the lateral masking paradigm are consistent with the hypotheses that lateral connectivity within early visual areas is atypical in autism, and may be considered a possible early neural origin for altered perception in autism.

**138.026 26** Atypical Medial Prefrontal Cortex Response to Implicit Emotion Processing in Autism Spectrum Disorders. B. S.

Copeland*[1], M. A. Patriquin[2], B. Wicker[3], M. M. Channell[4] and R. K. Kana[1], (1)*University of Alabama at Birmingham*, (2)*University of Houston*, (3)*Université Aix-Marseille*, (4)*University of California, Davis*

Background: Inferring others' emotions and intentions is critical in successful social interaction. Many individuals with autism spectrum disorders (ASD) struggle in navigating the social world, largely due to difficulty reading others' emotions from faces (Harms et al., 2010) and from body postures (Hadjikhani et al., 2009). Nevertheless, such difficulty may be less pronounced when the emotion is explicit and more pronounced when the emotion is implicit. This difference and its neural bases have been relatively under-examined in ASD. The fMRI study reported here uses dynamic action scenarios to examine the neural mechanisms underlying explicit and implicit emotion processing in ASD.

Objectives: The purpose of this fMRI study was to examine the brain activation and functional connectivity differences associated with implicit emotion processing in individuals with ASD and typically developing (TD) control participants.

Methods: 17 high-functioning adults with ASD (mean age = 24.5) and 15 TD adults (mean age = 24.7) watched a series of short videos (average length = 10 seconds) in a Siemens 3T MRI scanner. The videos, presented in an event-related design, consisted of an action or social interaction involving either one actor or two actors (emotions: happy, sad, angry, and afraid). Participants were asked to either determine the emotional state of an individual (explicit emotion processing) or to identify a specific object in the video (implicit emotion processing). There was also a control condition, where participants watched neutral videos and were asked to make a perceptual judgment. The fMRI data were analyzed using SPM8 (Statistical Parametric Mapping) software.

Results: Statistically significant group differences in brain activity were seen only during implicit emotion processing, with participants with ASD showing reduced activity, relative to TD participants, in medial prefrontal cortex (MPFC) and bilateral superior temporal sulcus ($p=0.001$; cluster size $=72mm^3$). Functional connectivity analysis revealed significantly weaker connectivity between several networks in the ASD participants during implicit emotional processing, especially the connections between MPFC and other regions like amygdala, STS, IPL, and fusiform gyrus. Behavioral analyses revealed that the ASD participants performed explicit emotion processing equally well as the TD control participants. However, the ASD participants made significantly more errors, compared to TD controls (ASD mean=70%; TD mean=91%), making non-emotion judgments during implicit emotion processing [$t(30)=2.3$; $p < 0.05$].

Conclusions: The findings of this study underscore the importance of MPFC in emotion processing. Decreased activation and connectivity of the MPFC, along with decreased performance in non-emotion judgment during implicit emotion processing in the ASD group suggest impairments in autism in the neural circuitry underlying automatic processing of emotions. The MPFC is a crucial brain region for implicit emotional processing; the connectivity of MPFC with amygdala has been found to be critical in emotion regulation (Zink et al., 2010).

**138.027 27** Atypical Neural Response to Perceptual Saliency in Children with ASD. C. J. Vaidya*[1], X. You[2], M. Norr[2], E. R. Murphy[2], W. D. Gaillard[1] and L. Kenworthy[1], (1)*Children's National Medical Center*, (2)*Georgetown University*

Background: Atypical top-down control and bottom-up perceptual processing has been posited to contribute to socio-emotional and cognitive deficits in children with Autism Spectrum Disorder (ASD). The top-down or goal-driven control of attention engages the dorsal attention network comprising superior frontal and dorsal parietal regions whereas the bottom-up or stimulus-driven capture of attention engages the ventral attention network comprising temporo-parietal junction and inferior frontal cortex.

Objectives: To examine the two attention networks, functional magnetic resonance imaging (fMRI) was performed while ASD and control children performed an ongoing task, in the context of novel or familiar distractors which appeared unexpectedly (bottom-up condition) or under monitoring/response instructions (top-down condition).

Methods: Eighteen 8-14 year old ASD and 22 control children with same age, gender and IQ distribution underwent two fMRI runs during a sustained attention task in which they pressed a button with their right hand for a triangle (target

stimuli) among serially presented squares, circles, and rectangles. In both runs, distracters (small flickering shape) were flashed in the periphery, which were either Familiar (high frequency) or Novel (rare). In the bottom-up run, distractors were unexpected as children were not forewarned, whereas in the top-down run, they had to monitor for a target distractor and respond with their left hand while performing the central task with their right hand.

Images were slicetime and motion corrected, normalized to EPI template and resliced to 3mm, smoothed with 8mm FWHM in SPM8. Contrasts of interest were Novel vs. Null, and Familiar vs. Null. The effects of any residual micromovements were removed by including six motion parameters and framewise displacement as regressors in the single subject-level analysis. For each run separately, subject-specific contrast maps were entered into separate ANOVAs in SPM8 with Group and Condition as categorical variables and age and FIQ as covariates of no interest, with interaction examined at $p<.005$, 10 voxels within an anatomical mask including regions of the ventral and dorsal attention system.

Results: During bottom-up attention, ventral attention regions in left inferior frontal cortex (BA 47 and 46), were more responsive to Familiar than Novel distractors in ASD children whereas they were more responsive to Novel than Familiar distractors in control children. Further, dorsal attention regions in parietal cortex (inferior and superior, BA 7) were also more responsive to Familiar distractors in ASD children, whereas they were equally responsive to both Novel and Familiar distractors in control children. During top-down attention, a dorsal attention region in frontal cortex (BA 6), was more responsive to Familiar than Novel distractors in ASD children.

Conclusions: The ventral and dorsal attention networks were engaged qualitatively differently in ASD and control children such that they were driven by familiarity rather than by novelty.

**138.028 28** Atypical Ventral Premotor Cortex Activity during Motor Imitation in Children and Adolescents with Autism. H. M. Wadsworth*, S. Sivaraman, C. Martin and R. K. Kana, *University of Alabama at Birmingham*

**Background:** Deficits in imitation have been widely reported in children and adolescents with autism spectrum disorders (ASD) (Rogers & Pennington, 1991; Williams et al., 2001). Recent evidence from neuroimaging research on imitation in autism points to the dysfunction of mirror neurons (Williams, 2008; Bernier and Dawson, 2009), although some studies report normal movement selectivity with no mirror neuron dysfunction in autism (Dinstein et al., 2010). While activity of the mirror neuron system (MNS) has been studied relatively more, the connectivity among the different nodes of MNS has been less explored (Kana, Wadsworth, & Travers, 2011). Thus, this fMRI study examined the MNS responses underlying motor imitation in children with autism.

**Objectives:** The primary goal of this project was to examine the nature and extent of MNS response in high-functioning children and adolescents with autism during motor imitation.

**Methods:** Participants included 12 high-functioning children and adolescents with autism (HFA) and 15 age-and-IQ-matched typically developing children (TD) (right-handed, 8-17 years of age). Participants took part in 2 separate sessions: 1) Assessment; and 2) MRI scanning. During the first session, the participants completed a series of neuropsychological tests, such as attention, and IQ. In the fMRI scanner, participants were asked to imitate a series of 20 high-resolution snapshots of hand actions performed by a model. These images were displayed at the center of the screen, one at a time for a period of 4000ms with an inter-stimulus interval of 6000ms in an event-related design. Participants were instructed to use their right hand to imitate the same hand action displayed in the picture. The fMRI data collected from a Siemens 3 tesla scanner were analyzed using SPM8.

**Results:** Both participants with an ASD and TD controls showed activation in the core regions of the MNS (posterior parietal, and ventral premotor cortex) while performing the motor imitation task. Between-group analysis of brain activation revealed significantly less activity in participants with autism, relative to TD controls, in the ventral premotor aspect of the MNS, but not in the posterior parietal area ($p=0.001$, 10 voxel extent threshold). In the assessment scores, we found participants with autism performing worse than TD controls in the Beery Visual-Motor Integration (VMI) task [$t(25)=2.06$; $p = 0.05$]. In addition,

the nonverbal cognitive scores (as measured by the WASI-2), which was higher for the ASD group, did not have a significant impact on brain activity as evident from a multiple regression analysis.

**Conclusions:** The results from this study are consistent with recent findings suggesting that the MNS as a whole system may not impaired in individuals with ASD (Cook & Bird, 2012). As such, these results suggest further examination of the specific role of each node of this system in the imitation deficits found in individuals with ASD. This may provide specific avenues to target for intervention. In these lines, future analyses for this study include an examination of the functional and effective connectivity, and examining brain-behavior relationships.

**138.029 29** Electrophysiological Assessment of Low-Contrast Visual Function and Neural Noise in Children with Autism Spectrum Disorder. P. M. Weinger*[1], V. Zemon[2], L. Soorya[3], A. Kolevzon[1], J. D. Buxbaum[1] and J. Gordon[4], (1)*Icahn School of Medicine at Mount Sinai*, (2)*Yeshiva University*, (3)*Rush University Medical Center*, (4)*Hunter College*

Background: Hyper- and hypo-reactivity to sensory input is now included in the DSM-5 as a core deficit of autism spectrum disorder (ASD). Previous studies, based on parent-report questionnaires, indicate that sensory symptoms are significantly more prevalent in children with ASD (60-90%) as compared to children with other developmental delays and typically developing controls. Furthermore, younger children who are more severely affected have the greatest number of sensory symptoms. Electroencephalograms (EEG) offer an objective method to assess sensory processing; however, lower-functioning populations are often difficult to test using conventional EEG methods, which usually involve long-duration runs, many electrodes applied to the head, and behavioral tasks. The current study explores the feasibility of single-channel EEG recording to investigate neural mechanisms and pathways associated with low-contrast vision and neural noise in children with ASD.

Objectives: (1) To assess the integrity of low-contrast responses in ON- and OFF-cell pathways (presumably within the magnocellular system) and (2) to assess the level of neural noise within the visual cortex of children with ASD.

Methods: Visual evoked potentials (VEPs) were obtained from children with ASD and typically developing controls by extracting the VEP from the ongoing EEG using a single electrophysiological channel comprised of three electrodes placed on the midline of the scalp. Stimulus conditions included contrast sweeps of bright or dark isolated-checks with appearance/disappearance sinusoidal modulation (12.5 Hz) to examine ON and OFF pathways, respectively. Contrast increased in 1-s octave steps from low to high levels. Each swept-parameter condition consisted of ten 7-s runs. ASD diagnoses were determined based on standardized research diagnostic instruments (ADOS, ADI-R) and DSM-5 criteria.

Results: Children in the ASD group displayed deficits in low-contrast responses to both bright- and dark-check stimuli. These deficits were present across contrast levels (1,2,4,8,16,32%) for both conditions. Results also indicate that the ASD group had higher levels of neural noise than did the control group at low contrasts (< 8%) when significant responses (signal-to-noise ratios >1) were not obtained. The ASD group displayed a relatively constant level of noise across the range of contrasts used, whereas the control group displayed low levels of noise at low contrasts and increases in noise level at increasing contrasts. Thus, group differences in levels of neural noise were significant only under low contrast conditions in which responses were either absent (mean signals not above noise) or weak.

Conclusions: Results provide electrophysiological evidence for deficits in low-contrast (magnocellular-biased) visual function and increased neural noise in children with ASD. This study also demonstrates the feasibility of short-duration, single-channel VEP recording in children at various levels of cognitive and behavioral functioning. VEPs hold promise as a rapid and reliable biomarker of early-stage visual processing deficits in ASD. Future studies must assess whether these findings persist in larger samples and whether abnormalities in basic low-level/non-social stimuli may translate into higher-order perceptual differences.

**138.030 30** Evidence for Distinct Neural Endophenotypes of Executive Dysfunction in Autism and Phenylketonuria. K. R. Bellesheim*, J. P. Stichter, K. E. Bodner, J. L. Sokoloff and S. E. Christ, *University of Missouri*

Background: Phenylketonuria (PKU) is a neurodevelopmental disorder characterized by a

deficient ability to metabolize the amino acid phenylanine, resulting in neurotransmitter dysregulation and white matter pathology. Similar to Autism Spectrum Disorder (ASD), the behavioral phenotype of PKU includes impairments in executive function and social communication (Baieli et al., 2003; Christ et al., 2010). Furthermore, PKU has historically also been considered as one of the potential causes of ASD (Friedman, 1969). It remains unclear, however, to what extent these disorders (and their associated executive dysfunction) are characterized by similar versus distinct neural endophenotypes.

Objectives: Functional magnetic resonance imaging (fMRI) methodology was used in conjunction with a non-verbal working memory task to compare and contrast the neural endophenotype associated with ASD and PKU.

Methods: A sample of 22 individuals with ASD (mean age = 13.1 years), 11 individuals with PKU (mean age = 25.0 years), and a combined comparison group of 24 neurologically intact individuals without PKU or ASD (mean age = 18.2 years) participated. Scans were obtained on a 3T Siemens Trio scanner with a standard 8-channel head coil. Stimuli were displayed using an LCD projector, and responses were recorded using a fiber optic switch. Neural activity was assessed while participants performed an n-back working memory task using novel face stimuli. The n-back working memory task included two conditions: 2-back and 0-back. In the 2-back condition, participants were shown a series of novel face stimuli one at a time and were instructed to respond when the current stimulus was the same as the stimulus that appeared two items prior. For the 0-back condition, participants were again shown a series of face stimuli; however, in this instance, they were asked to simply respond when they saw a pre-specified target stimulus. Each participant completed two functional runs including 6-8 counterbalanced task epochs (3-4 per condition).

Results: Consistent with past studies (e.g., Koshino et al., 2008), we found ASD-related abnormalities in neural activation in prefrontal regions including anterior cingulate cortex (ACC) as well as left and right dorsolateral prefrontal cortex (DLPFC) [$t(33) > 3.35$, $p < .005$ in all instances]. PKU was also associated with atypical neural activation of left DLPFC [$t(20) = 2.36$, $p = .03$]; however, the pattern of activation differed from that observed in the ASD group. Specifically, ASD was associated with decreased activation of left DLPFC compared to the healthy comparison group whereas PKU was associated with increased activation.

Conclusions: Although the general loci of the executive impairment (i.e., prefrontal cortex) are similar between the PKU and ASD, the precise pattern of activation differs. Whereas these two disorders may share a similar behavioral phenotype, the underlying neural endophenotype is distinct for each disorder.

**138.031 31** Examining Habituation in ERP Responses to Auditory Processing in Children with Autism. S. E. Schipul*[1], G. T. Baranek[1], F. C. Donkers[2] and A. Belger[1], (1)*University of North Carolina at Chapel Hill*, (2)*Tilburg University*

Background: Unusual sensory experiences are increasingly identified as a key characteristic of individuals with autism spectrum disorder (ASD)(Baranek et al., 2006), and have been included in the diagnostic criteria for the disorder in the Diagnostic and Statistical Manual V (American Psychiatric Association, 2013). In previous work, we examined event-related potential (ERP) responses to auditory stimuli in children with ASD and matched neurotypical children and found attenuated neural responses in ASD (Donkers et al., in press). However, the adaptability of these neural processes in ASD remains to be examined. In neurotypical individuals, ERPs have been shown to habituate (or attenuate) in response to repeated presentations of stimuli (e.g., Romero et al., 1996), reflecting adaptation to external sensory stimuli. Previous functional magnetic resonance imaging research has shown evidence of impaired neural adaptation in adults with ASD (Schipul et al., 2012). Here, we sought to determine if neural habituation, as reflected in ERP responses, is impaired in children with ASD.

Objectives: The current study examines changes in ERPs in response to repeated presentation of auditory stimuli in children with ASD and matched neurotypical (NT) children, in order to gain insight into the adaptability of neural processes in this population.

Methods: Participants include children with ASD and NT children (4-12 years of age). ERPs were

collected during a passive listening task, consisting of 5 blocks of standard tones and intermittent novel sounds. Data was collected from 11 electrode sites and was analyzed using EEGLab and FieldTrip MATLAB functions. ERP components examined include (1) the P1, reflecting early sensory processes; (2) the N1/N2, reflecting pre-attentive perceptual processes; and (3) the P3a, reflecting post-sensory attentional processes. ERPs were compared between blocks 1-2 and blocks 4-5 of the experiment in order to assess change over time.

Results: Preliminary results suggest that the NT group (n=10) shows greater changes over time in the P3a in response to novel sounds, as compared to the ASD group (n=10). This finding suggests that children with ASD show less habituation in attentional orienting processes in response to novel stimuli. Group differences are not significant with this sample size in the earlier, sensory ERPs to standard tones (P1, N1/N2). Final analyses will include data from an additional 18 children with ASD and 27 NT children that has already been collected, increasing power to find differences in the P1 and N1/N2, which are characterized by smaller effect sizes.

Conclusions: These preliminary findings suggest reduced habituation in attentional ERP responses to auditory stimuli in ASD, possibly reflecting reduced neural adaptability in the disorder. This work suggests that children with ASD may be less able than NT children to adapt to repeated sensory stimuli, which may have implications for our understanding of sensory hyperresponsivity in ASD. Further analyses with our complete sample size will have more power to examine habituation effects in earlier, sensory neural processes (P1 and N1/N2 ERPs). This work has the potential to inform our understanding of the adaptability of neural responses in children with ASD, which in turn may impact treatment.

**138.032 32** Gaze Contingent Games to Modify Neural Response to Eye Contact in ASD. A. Naples*[1], R. Tillman[2], E. Levy[2], H. S. Reuman[2] and J. McPartland[2], (1)*Yale Child Study Center*, (2)*Yale University*

Background: Decreased eye contact represents a common manifestation of social dysfunction in autism spectrum disorder (ASD). Prior electrophysiological research on gaze perception in ASD has focused on passive observation of social information, failing to address the interactive nature of eye contact. This research has identified atypicalities in event-related potential (ERP) indices of face processing in individuals with ASD. Behavioral treatments designed to improve eye contact are resource intensive. Automated intervention methods, such as computer games, are potentially more efficient but have historically lacked the contingency and synchrony that characterize true social interactions and are considered requisite for social skills treatments.

Objectives: The current study integrated eye tracking (ET) and electroencephalographic (EEG) recording in the context of an interactive, gaze-mediated computer game with the goal of modifying neural responses to reciprocal eye contact in ASD. We predicted that (1) eye movements to faces and gaze-cued objects would change in the context of a rewarding game and that (2) neural responses to faces and eyes would be enhanced as the game shaped more appropriate gaze behavior.

Methods: EEG was recorded from 10 high-functioning adolescents with ASD (mean age = 13.3) and 10 matched TD controls (mean age = 14.9) using a 128 electrode net. ET was recorded with a remote eye tracker (Eyelink-1000). Trials began with a peripherally-presented crosshair followed by a centrally-presented face. Contingent upon the participant's fixation, the face responded by looking at the participant or looking to a target in one of four corners of the screen. Participants earned points for maintaining eye contact or following gaze. ERPs were time-locked to face movement; the N170 was extracted from occipital electrodes and the P300 was extracted at central electrodes.

Results: Individuals with ASD displayed an attenuated N170 response to eye movement relative to TD peers (-.08μV versus -6.0μV , respectively) and failed to display differential neural response to direct versus averted gaze. TD individuals exhibited more negative N170s (-3.2μV) compared to individuals with ASD (-1.9uV) when viewing faces with reciprocal gaze. ET indicated that, overall, individuals with ASD looked less to the eyes than TD participants ($p$ =.01). Compared to TD counterparts, individuals with ASD looked between rather than at the eyes ($p$ = .08), and they did not show an expected bias to look to the eye contralateral to their dominant

eye ($p$=.016). Analyses in progress investigate gaze shift and neural response to eye contact across game trials.

Conclusions: Results revealed a marker of shared gaze that is attenuated in individuals with ASD. Individuals with ASD displayed reduced sensitivity to socially relevant changes in gaze even when these changes were contingent on their own behavior. Specifically, individuals with ASD showed reduced fixation to the eyes; however, even when looking to the eyes, they exhibited aberrant patterns of brain activity. This experiment holds promise for (1) evaluating the utility of automated, socially interactive behavioral interventions and (2) assessing brain activity during intervention, with the potential to modify interventions in-vivo in response to brain activity and behavior.

**138.033 33** Hand and Foot Action Perception in Autism. M. Thioux*[1], J. Suttrup[1], V. Gilmont[2], A. van der Wal[2], Y. Han[3] and C. Keysers[1], (1)*Netherlands Institute for Neuroscience*, (2)*University Medical Center Groningen, Rijksuniversiteit Groningen*, (3)*University of Groningen*

Background:

Most mirror neurons in monkey demonstrate only a broad congruence between observed and executed actions (e.g. a neuron firing during the execution of a precision grip will respond to the observation of the object being grasped with the mouth or foot). These broadly congruent mirror neurons are though to encode the goal of perceived actions irrespective of the mean used to accomplish the action. About 1/3rd of mirror neurons however fire solely when the observed action is performed the same way as during execution. These strictly congruent mirror neurons may encode the mean used to accomplish a goal (e.g. with the hand or foot).

Objectives:

Testing whether individuals with autism re-enact both the goal and the mean of others' actions in parietal and premotor cortices

Methods:

Sixteen participants with autism and 18 controls matched for age, IQ, and handedness watched short movies of hand and foot actions while their cerebral activity was recorded in a 3T MRI scanner (EPI sequence with TR=2s, TE=28ms, 39 slices 3.5mm thick). Participants watched 16 blocks of hand and 16 blocks of foot actions. Hand and foot actions were performed on the same objects with the same goal (e.g. squishing a foam ball), and were paired-matched for duration. At the second level, age, laterality and IQ scores were used as cofactor in a mixed design model with factors group and effector. SPMs were thresholded at P < 0.001 uncorrected, and activity in regions of interests was tested with P-FWE=0.05. Sleepiness was monitored with a camera during the entire session and evaluated on a 10-point scale. Participants' attention to the movies was further evaluated with 24 questions presented at the end of the scanning session.

Results:

Participants in both groups were well awake during the movies (9/10) and answered the verification questions with the same accuracy. In both groups, large portions of the parietal and premotor cortices were equally active during the perception of hand and foot actions. In addition, both groups showed similar effector effects in parietal lobe hand and foot regions. Finally, a significant interaction between group and effector was found in the left inferior frontal gyrus, where there was more activity for hand than foot in autism, but more activity for foot than hand in controls.

Conclusions:

The results so far suggest that individuals with autism activate the mirror neuron system like typically developing subjects during action perception. However, there might be subtle differences in the activation of strictly congruent mirror neurons involved in encoding the mean used to accomplish an action.

**138.034 34** Heart Rate Variability during Sleep in Children with Autism Spectrum Disorders. R. Harder[1], A. Diedrich*[1], F. Baudenbacher[1], A. Halbower[2], L. Goodpaster[1], S. E. Goldman[3], D. B. Fawkes[1], L. Wang[1], Y. Shi[1] and B. A. Malow[3], (1)*Vanderbilt University*, (2)*Children's Hospital Colorado Pulmonary Medicine*, (3)*Vanderbilt University Medical Center*

**Background:**

Studies have implicated autonomic nervous system dysfunction in autism spectrum disorders (ASD), including alterations in heart rate at baseline. Alterations in autonomic activity during

sleep in children with ASD have received less attention, despite an evolving literature on the importance of sleep for restoring homeostatic function.

**Objectives:**

The objective is to study heart rate and heart rate variability during sleep in children with ASD.

**Methods:**

We studied 24 children with ASD, with age of 7.7±1.9 years (mean ± standard deviation, SD) and 23 typically developing medication-free children (TD med-free) with age 8.0±1.9 years, who underwent overnight polysomnography including heart rate monitoring in the Vanderbilt or Colorado Clinical Research Centers.

Automatic R-R peak detection in electrocardiogram with manual verification was performed. Heart rate (HR) and heart rate variability (HRV) was computed for each sleep stage (W, N2, N3, and REM) in the first sleep cycle. HRV spectral components were calculated for low frequency (LF), high frequency (HF), and the LF/HF ratio based on common standards (TASK FORCE 1997). Multivariate statistical tests were performed with adjustment for age. Significance was set at p = 0.05.

**Results:**

HR decreases with onset of sleep, with minimum heart rate during N2 sleep, and increases during REM sleep in TD as well in ASD. Children with ASD had a similar heart rate dynamic during sleep but with a significant offset of higher heart rates through all sleep stages (median HR in bpm with $25^{th}$-$75^{th}$percentile ASD vs. TD for W: 85.05 (79.07-89.58) vs. 86.77 (83.58-94.95), N2: 70.16 (66.89-77.47) vs. 76.19(71.10-87.50) $p<0.05$, N3: 72.19 (69.85-81.10) vs. 78.93-(73.78-88.13) $p<0.05$, REM: 74.46(70.41-83.70) vs. 80.91(76.04-87.29) $p<0.05$).

Absolute LF power of HRV decreases during N3 and increases during REM. Children with ASD had a lower increase and lower power during REM (median LF in $msec^2$ with $25^{th}$-$75^{th}$percentile ASD vs. TD for W: 696.44(462.10-1269.49) vs. 806.00 (389.15-1327.63), N2: 742.23(472.00-1154.58), N3: 377.36 (212.95-732.901) vs 314.11(154.06-856.07), REM: 643.94 (437.51-918.24) vs. 894.50 (574.80-2130.664) $p<0.05$). No significant differences could be detected for HF, and LF/HF ratio.

LF and HF power increases with age in TD and ASD for wake. For REM, ASD showed a tendency of lower increase of LF and no change in HF with increasing age.

**Conclusions:**

Children with ASD showed higher heart rates during sleep and wakefulness. Analysis of HRV showed an abolished increase of LF during REM sleep, which could indicate a possible lack of sympathetic activation during restorative REM sleep in children with ASD. Age dependent changes in HRV during REM sleep are abolished for LF or not present for HF in ASD. This could indicate that the sympathetic and vagal branch of the autonomic system is affected during aging in ASD. Therefore, parameters of HRV during REM sleep are a potential biomarker of developmental trajectory and may be used to detect early signs and progression of ASD.

**138.035 35** Hippocampal-Parietal Hyper-Connectivity Predicts Visual-Spatial Abilities in Children with Autism. M. Rosenberg-Lee*[1], L. Q. Uddin[1], S. Qin[1], D. A. Abrams[1], P. Odriozola[1], J. M. Phillips[2], C. Feinstein[1] and V. Menon[1], (1)*Stanford University*, (2)*Stanford University School of Medicine*

Background:

Autism spectrum disorders (ASDs) are often accompanied by an uneven profile of cognitive capacities. From rare reports of savant skills to the consistent finding of stronger performance than verbal IQ, spared and enhanced abilities in autism tend to involve veridical memory and visual-spatial processing. While little is known regarding the neural underpinnings of enhanced abilities in children with autism, these areas of strength point towards the involvement of medial temporal and parietal lobe structures. Resting state functional MRI provides a powerful method for probing intrinsic connectivity between brain regions. Recent studies using the method have revealed a conflicting picture of both hypo- and hyper-connectivity in individuals with ASD relative to typically developing (TD) peers.

Objectives:

We sought to understand whether patterns of intrinsic functional brain connectivity in children with ASD could be related to cognitive strengths. We focused on connectivity of the hippocampus, an area critically involved in memory and spatial navigation.

Methods:

Six minutes of resting state functional MRI was collected in 20 children (aged 7-12) with ASD and 19 TD children, matched on age, IQ, and gender. We compared functional connectivity between groups from left and right anterior hippocampal seeds, an area implicated in binding multiple visual-spatial features. Parent report of exceptional abilities from the ADI-R were used to compare connectivity measures amongst children with ASD. Support vector regression (SVR) was used to probe whether areas differing in hippocampal connectivity could predict verbal IQ (VIQ) and performance IQ (PIQ) in TD children and children with ASD.

Results:

Children with ASD displayed patterns of both hypo- and hyper-connectivity of the hippocampus with other cortical and subcortical regions. TD children had greater connectivity of the hippocampus to the posterior cingulate, ventral medial prefrontal cortex and parahippocampal gyrus, all areas implicated in the default mode network and self-related processing. In contrast, children with ASD had greater connectivity from right hippocampus to the right intraparietal sulcus and the adjoining angular gyrus, areas implicated in visual-spatial processing. Hippocampal-parietal connectivity was strongest in children with ASD whose parents reported they had exceptional visual-spatial abilities. SVR analyses revealed that the pattern of hippocampal connectivity in this parietal cluster could predict PIQ scores for children with ASD but not for TD children. Hippocampal-parietal connectivity did not predict VIQ for either group.

Conclusions:

These results suggest that hippocampal-parietal hyper-connectivity in children with ASD is related to spared and enhanced non-verbal intelligence and visual spatial abilities in these children.

**138.036 36** Imaging of the Autism Brain and Surrounding Tissues Using Linear 2D Transcranial Ultrasonography. J. J. Bradstreet*[1], M. Ruggiero[2] and S. Pacini[2], (1)*Newport Brain Research Laboratory*, (2)*University of Firenze*

Background: Autism spectrum disorders (ASDs) are developmental conditions of uncertain etiology which have now affected more than 1% of the school-age population of children in many developed nations. Cortical abnormalities observed from autopsy specimens, including inflammation and structural aberrations, have been inconsistently reported. Recently, serial brain magnetic resonance imaging studies from near birth to 2 years of age were noted to be highly predictive of autism when increased frontal extra-axial fluid remained persistent. Transcranial ultrasonography (TUS) via the temporal bone acoustical window appeared to be a potential method of investigation to determine the presence of both cortical abnormalities and increased extra-axial fluid (EAF).

Objectives: To evaluate the brain of children with autism and their siblings using 2D TUS.

Methods: TUS was accomplished using a linear probe typically used for musculoskeletal investigations (10-5 MHz). Multiple images were recorded and real-time measurement of the cortex and extra-axial spaces were accomplished. Specifically, anatomical areas of significance to autism (primary language and auditory cortical locations) are readily imaged with this novel ultrasonographic technique. With this initial cohort, parents volunteered 18 ASD subjects (males =17) for evaluations (all ages < 16, mean = 7.81 years + 2.4 years), and 12 neurotypical siblings were also examined (all ages < 21, mean = 8.89 years + 3.82 years). Childhood Autism Rating Scale, Second Edition, (CARS2®) scores were obtained as a routine in the practice and the ASD score mean was 48.65 + 7.32 (Severe).

Results: Comparisons of the extra-axial spaces indicated increases in the ASD subjects. For EAF we scored based on the gyral summit distances between the arachnoid membrane and the cortical pia layer (subarachnoid space): 1) <0.05 cm, 2) 0.05 – 0.07 cm, 3) 0.07 – 0.10 cm, 4) > 0.10 cm. All of the neurotypical siblings scored 1, whereas the ASD mean score was 3.31 + 0.7. We also defined cortical dysplasia as the following: hypoechoic lesions within the substance of the cortex, or disturbed layering within the grey

matter. For cortical dysplasia we scored: 1) none observed, 2) rare hypoechogenic lesions and/or mildly atypical cortical layering patterns, 3) more common, but separated areas of cortical hypoechogenic lesions, or more commonly abnormal cortical layering, 4) very common or confluent areas of cortical hypoechogenicity and/or markedly disturbed layering of the cortex. Again all of the neurotypical siblings scored 1, while the ASD subjects' mean score was 3.0 + 0.92.

Conclusions: These initial TUS observations are consistent with and extend the age range of previous MRI observations of increased EAF in ASDs. The new real-time observations of hypoechogenic lesions in the cortical grey matter suggest focal cortical disruption in areas critical to both language and auditory processing (core features of autism). TUS may be a useful screening technique for ASDs which, if confirmed with repeated studies and high resolution MRI, provides rapid, noninvasive qualification of EAF and cortical lesions.

**138.037 37** Impaired Maturational Changes of Network Organization in ASD: An Ica Study Using Resting State fMRI. M. Sullivan*, I. Fishman, Y. Cabrera and R. A. Müller, *Dept. of Psychology, San Diego State University*

Background: Converging evidence indicates that brain abnormalities in autism spectrum disorders (ASD) involve atypical network connectivity, yet the particular connectivity patterns and the extent to which they deviate from those seen in typical development are currently debated. While there is evidence supporting both greater and weaker brain network connectivity in individuals with ASD, as compared to their typically developing (TD) peers, the developmental framework emphasizing age-associated changes in connectivity is often overlooked, or altogether ignored.

Objectives: To examine developmental trajectories of network connectivity in a sample of children and adolescents with ASD, as compared to TD controls. Specifically, recent findings suggest that, while typical development is associated with increasingly segregated (weaker between-network connectivity) and increasing integrated (greater within-network connectivity) brain networks, this pattern appears to be disrupted in ASD. The aim of this project was examine this notion using a data-driven, model-free approach to quantify large-scale patterns of functional connectivity (i.e., functional networks) in children and adolescents with ASD.

Methods: Resting-state functional MRI (rs-fMRI) data (acquired for 6:10 minutes) from 28 children and adolescents with ASD (ages 7-18 years old) and 33 TD participants, matched on age, gender, non-verbal IQ, and head motion, were included. Utilizing publicly available templates of major functional brain networks (Smith et al., 2009) generated through Independent Component Analysis (ICA) of rs-fMRI data, we applied the dual regression approach implemented in FSL to decompose each participant's BOLD data into 10 functional networks, also known as independent components. The dual regression algorithm was applied to identify both participant-specific time courses and spatial maps corresponding to the 10 brain networks. Z scores associated with each network were then compared between groups (with a two-sample t-test), as well as correlated with age within each group.

Results: We observed significantly different functional connectivity within several large-scale brain networks in children and adolescents with ASD, relative to TD controls. Namely, greater connectivity was found for the visual/medial, visual/occipital pole and the cerebellar networks. Moreover, we found differential age slopes of functional connectivity between TD and ASD groups. Some networks (e.g., two visual networks) showed significant reduction in connectivity with age in the TD group, but no association with age in ASD; others (such as default mode network) showed significantly increasing connectivity with age in TD participants, but no age effect in ASD.

Conclusions: Our findings suggest that large-scale functional brain networks have differential maturational trajectories in TD children and adolescents, with decreasing integration in visual networks, but increasing integration in DMN. The trajectories of network maturation appear to be disturbed pervasively in ASD, with many networks showing no significant age-related changes. Our findings underscore the importance of considering developmental trends and trajectories when characterizing brain network abnormalities in ASD.

**138.038 38** Mapping Human Brain Function with Diffuse Optical Tomography. A. T. Eggebrecht*, B. L. Schlaggar, S. E.

Petersen, J. N. Constantino, J. R. Pruett and J. P. Culver, *Washington University School of Medicine*

Background: Mapping human brain function has been transformative in systems neuroscience. However, traditional functional neuroimaging, with positron emission tomography (PET) or functional magnetic resonance imaging (fMRI), cannot be used when applications require portability, or are contraindicated because of ionizing radiation (PET) or implanted metal (fMRI). Optical neuroimaging offers a noninvasive alternative that is radiation free and compatible with implanted metal and electronic devices (e.g., pacemakers). However, optical imaging technology has heretofore lacked the combination of spatial resolution and wide field-of-view sufficient to map distributed high level brain functions.

Objectives: In this paper we present a large field-of-view high-density diffuse optical tomography (HD-DOT) system with anatomical modeling approaches that collectively provide new imaging capabilities and enable novel milestones for optical neuroimaging. Higher order brain functions, specifically area MT and language processing areas, are mapped using tasks as are a set of resting state networks (RSNs), including the default mode, dorsal attention, and fronto-parietal control networks.

Methods: Eight subjects underwent non-concurrent HD-DOT and fMRI sessions. The large field-of-view high-density DOT instrument, based on previous opto-electronic circuitry (Zeff et al., 2007), uses 96 optode source positions and 92 optode detector positions in an imaging array that wraps around the subject's head covering the occipital, parietal, temporal, and prefrontal cortex. Data was averaged across subjects and t-maps were created using one-sided random effects t-tests. Subjects were presented tasks to stimulate higher-order cognitive areas including visual area MT (static and moving dots; Swallow et al., 2003) and language processing areas (Petersen et al., 1988) associated with hearing, reading, speaking, and generation of words. Seed-voxel maps of functional connectivity were generated from resting state data (10 minutes; subjects fixated on a small cross on a screen and were instructed to think of nothing in particular). Pearson r-values were converted to Fisher-z vaues and were averaged across subjects.

Results: To measure higher order brain function, we first attempted imaging higher order visual processing in region MT. Non-concurrently recorded fMRI activations show strong correlation in their temporal response. Also, the regions detected show excellent spatial co-localization. Second, the language processing centers of the brain were broken down into sensory (visual and auditory), motor (motor mouth), and cognitive association areas (verb generation in Broca's area) with spatial correspondence between HD-DOT and fMRI. We believe this is the first reported mapping of the hierarchy of the language system with optical neuroimaging. Third, strong bilateral patterns of functional connectivity are co-registered between HD-DOT ΔHbO and fMRI BOLD RSN maps in the sensory motor networks. Additionally, in areas associated with higher order RSNs, function connections are evident not only between bilateral regions, but also between differentiable anterior-posterior constellations of regions. The seed-seed correlation values shows qualitative and quantitative agreement between the modalities.

Conclusions: Collectively these maps of tasks and resting state function in adult humans clearly indicate that high-density DOT can be a practical and powerful tool for functional brain mapping of children with Autism Spectrum Disorders.

**138.039 39** Network Sculpting Index Suggests Impaired Functional Network Differentiation in ASD. L. C. Andersen*[1], I. Fishman[2], C. L. Keown[1], A. Nair[3] and R. A. Müller[2], (1)*San Diego State University*, (2)*Dept. of Psychology, San Diego State University*, (3)*University of California San Diego*

Background: There is increasing consensus that ASD is a disorder involving distributed brain networks. Functional connectivity MRI (fcMRI) studies have produced mixed findings, including both underconnectivity and overconnectivity in ASD, implicating default mode network (DMN), mirror neuron system (MNS), and the mentalizing (Theory of Mind, ToM) network. Seemingly contradictory findings could reflect complementary aspects of impaired network sculpting, characterized by decreased connectivity within neurotypical networks and increased connectivity outside of these networks.

Objectives: To evaluate the efficiency of neurotypical networks (DMN, MNS, ToM) in ASD and typically developing (TD) groups by calculating a network sculpting index (NSI), a

ratio of within network connectivity and outside network connectivity.

Methods: Resting-state functional MRI data were acquired for 6:10 minutes for 33 children and adolescents with ASD (7-18 y/o) and 33 TD participants matched for age, motion, and non-verbal IQ. Standard preprocessing involved motion and field map correction, spatial smoothing, low bandpass filtering (.008<*f*<.08Hz), nuisance regression, and standardization to MNI152 template. For each network (DMN, MNS, ToM), regions of interest (ROIs) were identified using 6mm-radius spheres centered on previously reported coordinates (Van Overwalle & Baetens, 2009; Watanabe et al., 2012). Within-network masks were created for each ROI, including the seed and all other ROIs in the network (dilated to 12mm radius); outside-network masks excluded all network ROIs and non-cortical voxels. Individual whole-brain correlation maps (using average time series extracted from seed) were cluster corrected ($p<1^{-6}$) and Fisher-transformed to *z′*. For each network, the number of significant voxels, weighted by *z′*, was determined for within- and outside-network masks, and was then used to calculate the NSI using the formula: NSI = (WNC-ONC)/(WNC+ONC), with WNC and ONC being within and outside-of network connectivity, respectively.

Results: Mean NSI was significantly reduced in the ASD group ($p<.05$) for DMN whereas no significant differences were detected for MNS or ToM. A correlational analysis of NSI and three *a priori* selected social measures (ADI-Social, ADI-Communication, and ADOS Communication + Social [CS] scores available for ASD participants only) revealed a negative relationship between NSI and ADOS CS in MNS ($r$=-0.35, $p<.05$) and ADI-Communication scores in ToM ($r$=-.39, $p<.05$). Based on these correlations, a post hoc analysis was performed in a subset of ASD participants ($n$=25) with highest level of social symptomatology as defined by ADOS CS scores ≥10. Direct group comparison of this ASD subsample and 25 TD participants matched on age, motion, and non-verbal IQ corroborated earlier results in DMN (TD>ASD, $p<.05$). In addition, this analysis yielded significant between-group differences in mean NSI for MNS and ToM (TD>ASD, $p<.05$).

Conclusions: Findings suggest that DMN is less efficiently sculpted in individuals with ASD, compared to TD controls (more connectivity outside of the network than within). Concordant between-group differences were also found for MNS and ToM networks, but these were detected only in ASD participants with relatively high symptom severity.

**138.040 40** Neural Correlates of Affective Priming in ASD. A. Lartseva*[1], T. Dijkstra[2], C. Kan[1] and J. K. Buitelaar[3], (1)*Radboud University Nijmegen Medical Centre*, (2)*Radboud University Nijmegen*, (3)*Radboud university medical center*

Background: People take less time to evaluate a word as emotionally positive or negative if it is preceded by another word of the same emotional valence. This effect is called affective priming and is thought to reflect early bottom-up influence of emotional valence of the first (prime) word on the recognition of the second (target) word and on response preparation. There is some evidence that individuals with ASD process emotional stimuli differently, however, it is not clear whether this difference occurs at an early or later stage.

Objectives: To investigate behavioral and neural correlates of affective priming in ASD using reaction times (RT) and EEG.

Methods: Our aim is to recruit 20 participants with ASD and 20 matched healthy controls. Participants read prime-target word pairs on the screen and responded as fast as possible whether the target was emotionally positive or negative. Time interval between the onset of the prime and the target was 300 ms. In addition, we measured Autism Quotient (AQ) and Empathy Quotient (EQ) in all participants.

Results: Preliminary analysis (7 ASD and 14 controls) revealed that that priming effect for positive target words significantly correlated with AQ (Pearson's r=0.46, p<.05) and EQ (r=-0.47, p<.05). Priming effect for negative target words showed a marginal inverse correlation with AQ only (r=-0.39, p=.08). In other words, participants with ASD were significantly speeded up by affectively congruent positive primes, but less so by congruent negative primes. In the EEG data, target words preceded by an affectively incongruent compared to congruent prime elicited an increased Late Positive Component (LPC) amplitude in the time window between 500-700 ms. The magnitude of the LPC effect positively

correlated with AQ score of the participants. Looking at positive and negative words separately, we found that AQ score correlated significantly with the LPC effect for negative target words ($r=0.7$, $p<.01$), but not for positive words.

Conclusions: Participants with ASD seem to inefficiently process negative valence specifically. In participants with ASD, but also in controls with high AQ scores, presenting an emotionally negative prime did not lead to faster evaluation of negative targets, suggesting that it was either ignored or not processed in time. LPC amplitude which is associated with increased processing effort and deeper stimulus encoding was also found to correlate with AQ scores for negative targets only. While in participants with low AQ negative targets elicited high LPC amplitudes irrespective of the priming condition, in participants with high AQ congruent negative prime-target pairs elicited much lower LPC, suggesting that it was not efficiently encoded. We conclude that processing of negative emotion is impaired in ASD, while processing of positive emotion is relatively unaffected.

**138.041 41** Neural Correlates of Cognitive Control and Attentional Orienting in Adults with Autism Spectrum Disorders. D. S. Karhson* and E. J. Golob, *Tulane University*

Background:

Abnormal sensory reactivity is widely reported in people diagnosed with autism spectrum disorder (ASD). Appearing first in childhood and persisting throughout adulthood, abnormal reactivity is often observed as increased responsiveness in visual and/or auditory modalities. Data from cognitive neuroscience research suggests that changes in attention can alter sensory processing at several levels of analysis. Thus, abnormal stimulus-driven bottom-up processing could be contributing to atypical sensory reactivity. Restricted, fixated interest and intense focus might describe atypical functioning of voluntary top-down attentional control. Additionally, attentional pathways are modulated by the general cognitive factor and individual difference variable of working memory capacity (WMC). Defined as the amount of related information that can be actively maintained and manipulated in an accessible state, WMC contributes to the control cognition and modulating orienting responses. Electroencephalography will be used to investigate underlying cognitive processes with excellent temporal resolution, time-locked to stimulus presentation.

Objectives:

Current study measured event-related potentials (ERPs) associated with endogenous and exogenous orienting responses in participants with ASD after completing a modified 3-stimulus auditory oddball paradigm. Effects of sensory reactivity, perceptual load, and WMC on auditory cortical potentials to targets, non-targets, and distractors are examined.

Methods:

16 adults with ASD and 16 age- and IQ-matched control participants completed (recruitment is ongoing at abstract submission) the Adolescent/Adult Sensory profile and Kaufman Brief Intelligence Test (KBIT-2) prior to completing the auditory attention task. Electroencephalography was recorded as participants performed a modified 3-stimulus (target, non-target, and distractor) oddball task under varying perceptual load (high or low). Presented stimuli were random and binaural with an inter-stimulus interval of 2000 ms (~60dB, 200ms duration, 200 stimuli/block, 4 blocks/perceptual load, 8 blocks total). Infrequent pure tone targets (1000 Hz, probability = .12) and frequent non-targets (probability = .76) were presented at 0° midline. Sounds are not masked or presented concurrently with other auditory stimuli during the task, making discrimination based on sound source location or stimulus location possible. Presentation of white noise distractors at various spatial locations (-90°, 0°, or +90°; probability=0.12) and manipulation of non-target frequency (low load: 500Hz, high load: 950Hz) were used to vary perceptual load. ERPs examined reflect early sensory and attentional processes.

Results:

Preliminary analyses on the Adult Sensory Profile established atypical sensory reactivity in 9 ASD participants (4 female, mean age = 29.8) specifically for low registration, sensation seeking, and sensation avoiding items. ERP analyses suggest perceptual load was sufficiently modulated as evidenced by changes in N100 amplitude to variations in frequency. Components

associated with exogenous attentional orienting (P50 and P200) were modulated by perceptual load for non-targets. Whereas potentials associated with feature classification (N200) were robustly modulated by distractor location.

Conclusions:

Perceptual load may differentially modulate white noise and non-target auditory stimuli processing in ASD. Atypical sensory reactivity may contribute to perceptual load changes, but further analyses are required the relationship. Further evaluation is also needed to determine if effects are specific to ASD. Measures of cognitive control will be included to establish the influence of individual difference on ASD neural activity.

**138.042 42** Neurocognitive Factors Associated with Neural Specialization for Letters in ASD. A. Dominguez*[1], A. Naples[1], R. Tillman[1], E. Levy[1], H. S. Reuman[1], R. T. Schultz[2], A. Klin[3], L. Mayes[1] and J. McPartland[1], (1)*Yale University*, (2)*The Children's Hospital of Philadelphia*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

Background: Problems with neural specialization are hypothesized to negatively impact social function in ASD. However, recent evidence suggests that children with ASD display normative patterns of specialization for non-social information, such as letters of the alphabet, despite social impairments. Event related potentials (ERPs) demonstrate similar time course and morphology for specialized face and letter perception at occipitotemporal sites (N170). Neural and behavioral facets of social perception are well studied in ASD, but few studies have focused on factors related to preserved processing of letter and word-related information in ASD. Because some children with ASD display advanced skills and a high level of interest and proficiency in reading, understanding the brain bases of letter perception and their behavioral correlates holds potential to clarify areas of strength in ASD and potential strategies to target compensatory function.

Objectives: This study examined neural and behavioral correlates of letter processing in ASD. Our goals were to examine variability in neural responses to letters as a function of (a) performance on standardized assessment of phonemic decoding, (b) verbal cognitive abilities, and (c) use of verbal and written language in daily life.

Methods: Participants were thirty-six children with high-functioning ASD (*Mean age = 11.2 years)* and eighteen TD children (*Mean age = 12.6 years)* matched for sex, age, and IQ. ERPs were recorded with a 256 electrode Geodesic sensor net while participants completed a letter recognition task. ERP analysis focused on N170 amplitudes and latencies evoked by letter and pseudoletter stimuli. Reading ability was assessed with the Letter-Word Identification and Word Attack subtests of the Woodcock-Johnson Tests of Achievement-III; verbal IQ was measured by the Wechsler Abbreviated Scale of Intelligence. The Written Communication Subscale of the Vineland Adaptive Behavior Scales assessed writing skills of each participant. Circumscribed interest in reading was measured with the Yale Special Interest Survey.

Results: A main effect of condition indicated that both groups demonstrated shorter P1 latency ($F(1, 52) = 16.28$, $p \leq .01$) and increased amplitude of the N170 ($F(1, 52) = 14.67$, $p \leq .01$) for letters relative to pseudoletters. Single word reading ability was correlated with longer right hemisphere N170 latency in the letter condition ($r = .64$, $p \leq .01$). Preliminary analyses indicate positive correlations between ERP parameters and adaptive measures of written communication and verbal cognitive ability.

Conclusions: Individuals with ASD displayed normative patterns of specialization for letters of the alphabet, in terms of both strength and latency of neural response. Likewise, the performance of children with ASD on standardized tests of decoding was comparable to the control group and in the average range. This study demonstrates that variability in neural specialization of letters is associated with both laboratory and real-life functioning in ASD. Results suggest that investigations of areas in preserved function in ASD can inform development of interventions to (a) apply extant strengths to boost areas of vulnerability and (b) harness intact brain systems for compensatory function in ASD.

**138.043 43** Prenatal Testosterone Exposure and Hemispheric Asymmetry for Language and Spatial Memory: A Prospective Cohort Study. L. P. Hollier*[1], M. T. Maybery[1], J. Keelan[1], M. Hickey[2] and A. Whitehouse[3], (1)*University of Western Australia*, (2)*University of Melbourne.*, (3)*Telethon Institute for Child Health Research, The University of Western Australia*

**Background:**

Autism is among the most severe, prevalent and heritable of all neurodevelopmental disorders. However, the factors causing autism are still unclear. Any aetiological theory must incorporate a plausible explanation of the core cognitive abilities of individuals with autism. It has long been speculated that developmental language difficulties may reflect failure to develop typical lateralisation. Hemispheric differences for function are among the most replicated findings in all of neuropsychology. Typically, the most crucial areas involved in language production are found in the left hemisphere, while the right hemisphere is more specialized for visuospatial functions. It has been suggested that differing concentrations of prenatal testosterone may underpin variations in cerebral lateralisation. However, research in this area has been limited by indirect measures of cerebral lateralisation (i.e. handedness) and prenatal testosterone (i.e. 2D:4D digit ratio).

**Objectives:**

The aim of this study is to investigate whether levels of circulating testosterone are associated with hemispheric asymmetry for language and spatial memory, using functional Transcranial Doppler Ultrasonography (fTCD) to measure hemispheric asymmetry. fTCD uses ultrasound to measure the blood flow in the left and right middle cerebral arteries. It was hypothesised that higher fetal testosterone concentrations would be associated with reduced left hemisphere activation for language and increased right hemisphere activation for spatial memory. A secondary aim is to examine whether cognitive abilities in adulthood are related to variations in prenatal testosterone and hemispheric asymmetry.

**Methods:**

Umbilical cord serum testosterone concentration was used as a surrogate measure of prenatal testosterone exposure. Samples taken immediately after delivery in a subset of the Western Australian Pregnancy Cohort Study were assayed for testosterone by liquid chromatography-mass spectrometry. fTCD sessions were conducted with subset of male participants from the cohort (20 high umbilical testosterone; 20 low umbilical testosterone). Recordings were taken while the participants completed a word generation task and a visual short-term memory task. Participants also completed a number of tasks assessing verbal and non-verbal abilities.

**Results:**

A Laterality Index (LI) was calculated by computing the relative difference in blood flow velocity between the two hemispheres. No significant differences were found between the high and low testosterone groups for word generation LI, $t$ (38) = -.688, $p$ = .50, or spatial memory LI, $t$ (38) = -.244, $p$ = .81. Verbal and non-verbal ability was not significantly related to prenatal testosterone concentration or hemispheric asymmetry ($p$> .05).

**Conclusions:**

Results show no relationship between umbilical testosterone levels and hemispheric asymmetry for language or spatial memory. This is in contrast with previous research using various proxy measures. In addition, cognitive abilities in typically developing adults were not related to prenatal testosterone exposure or hemispheric asymmetry. The current study is the first to have used a neuroimaging technique, to measure hemispheric asymmetry, in conjunction with a relatively direct measure of prenatal testosterone exposure. The findings indicate that prenatal testosterone exposure may not be related to the development of cerebral lateralisation.

**138.044 44** Procedural Memory and Delta EEG Power during Nrem-Sleep in Young Typical and Autistic Adults. A. C. Rochette[1], E. Chevrier[1], I. Soulières[2], L. Mottron[3] and R. Godbout*[1], (1)*Sleep Laboratory & Clinic*, (2)*University of Quebec in Montreal*, (3)*Centre de Recherche de l'Institut Universitaire de Santé Mentale de Montréal*

Background: People with ASD are reported to perform poorly on sensory-motor procedural tasks when compared to typical participants (TYP). There is evidence suggesting that Stage 2 and Slow Wave Sleep (SWS) are linked to sensory-motor procedural learning. Moreover, Delta EEG activity, a slow EEG frequency band that characterizes SWS and that is also present during Stage 2, is thought to play a role in brain plasticity and formation of new learnings and memories.

Objectives: We verified if a relation exists between Delta EEG power on one hand, and sensory-motor procedural learning and performance on the other hand in ASD and TYP adult participants.

Methods: The sleep of 13 ASD and 14 TYP participants (22.1±3.8 and 21.5±3.6 years old, respectively) was recorded for 2 consecutive nights using a 22-electrode EEG montage. Spectral analysis of Delta (0.75-3.75 Hz) EEG power was obtained for stage 2 and SWS. A sensory-motor procedural task (Rotary Pursuit Task) was administered the morning following night 2. Learning and performance indices (i.e., increase of performance across trials and average performance for all trials, respectively) were calculated. Parametric and non-parametric correlation analyses were conducted to test the association between Delta EEG power during sleep and learning/performance.

Results: In the TYP group, we found a significant positive correlation between the learning index and Delta relative power during stage 2 sleep all over the scalp (Fp1, Fp2, F7, F3, Fz, F4, F8, T7, C3, C4, T8, Tp7, P3, Pz, P4, Tp8, and O2) and during SWS for the frontal and the left temporal regions (Fp1, Fp2, F7, F8, T7, Tp7, and O2). In the ASD group, Delta relative power and learning were correlated within the frontal and the left temporal regions during stage 2 (Fp1, Fp2, F7, T7, Tp7, and P7); no significant correlation was found during SWS. A significant positive correlation was found between the performance index and Delta relative power during stage 2 (F3, Fz, F4, C3, C4, T8, Cp5, Cp6, P4, Tp8) in the ASD group only.

Conclusions: These results suggest that Delta activity during sleep facilitates **learning** a sensory-motor procedural task in TYP as well as in ASD groups of participants. Delta activity, however, is positively associated with **performance** only in ASD. It suggests that sensory-motor procedural learning and performance of people with ASD do not rely on the exact same neuronal networks than TYP participants.

**138.045 45** Rest Cerebral Blood Flow in the STS Correlates with Social Perception Impairments in Children with ASD. A. Saitovitch*[1], E. Rechtman[1], H. Lemaitre[1], N. Chabane[2], R. Calmon[1], D. Grévent[3], A. Philippe[4], F. Brunelle[1], N. Boddaert[1] and M. Zilbovicius[1], (1)*Inserm Research Unit 1000 "Neuroimaging and Psychiatry"*, (2)*Inserm Research Unit 1000; Service de Pedopsychiatrie Hôpital Robert Debre*, (3)*Inserm Research Unit 1000; Necker Hospital*, (4)*Service de Génetique Hôpital Necker*

Background:

A lack of preference for relevant social features is one of the main clinical characteristics of ASD. During the last decade, the use of eye-tracking methodology has allowed an objective and quantitative characterization of this social perception deficit in children with ASD. In addition, several brain imaging studies have suggested that abnormalities within the superior temporal sulcus (STS) could be related to social impairments in autism.

Objectives:

In this study, we aimed to objectify social perception process in children with ASD using eye-tracking in order to investigate a putative correlation between social perception impairments and rest functional brain activity. For this purpose, MRI arterial spin labelling (ASL) was used to measure rest cerebral blood flow (rCBF).

Methods:

Thirty-two children with ASD diagnosis based on ADI-R (mean age = 7.7 ± 3.4) participated on this study and underwent an eye-tracking study followed by an MRI-ASL study. Tobii T120 eye-tracker was used to measure participant's number of fixations to the faces of the characters during passive visualization of social scenes. MRI-ASL was used to measure rCBF. Whole brain regression analyses were performed on the smoothed and normalized ASL images using number of fixations to the faces as covariate within SPM8 (http://www.fil.ion.ucl.ac.uk/spm).

Results:

ASL-MRI whole brain analyses showed a significant positive correlation between the number of fixations to the face and rest CBF in the right posterior STS ($p < 0.001$ uncorr). Children who looked less to the face of characters during visualization of social scenes where those who had the lower rest CBF values in the right pSTS.

Conclusions:

This results showed for the first time a correlation between a social behavior and a functional brain

activity at rest, even though the measurements were unrelated and performed separately. This correlation suggests that social behavior in children with ASD is associated with, and might be predicted by, the level of functional activity at rest within the STS.

**138.046 46** Sleep Patterns in Children with High Functioning Autism: Polysomnography, Questionnaires and Diaries in a Non-Complaining Sample. A. Lambert[1], S. Tessier[1], E. Chevrier[1], P. B. Scherzer[2], L. Mottron[3] and R. Godbout*[4], (1)*Sleep Laboratory & Clinic, Hop. Riviere-des-Prairies*, (2)*Universite du Quebec a Montreal*, (3)*Centre de Recherche de l'Institut Universitaire de Santé Mentale de Montréal*, (4)*Sleep Laboratory & Clinic, Hop. Riviere-des-Prairies, Universite de Montreal*

Background: Sleep patterns in children with autism are frequently only reported on questionnaires filled by parents.

Objectives: The aim of this study was to characterize sleep using objective and subjective measures in the same sample of autistic children without comorbidities and no primary complaints of sleep disorders.

Methods: Eleven autistic children (10.3 ± 2.2 years) diagnosed with ADI-R and ADOS criteria and 13 typically-developing children (10.2 ± 2.0 years) were recruited. Exclusion criteria comprised the use of psychotropic medication, a full IQ lower than 75, a history of epilepsy and spontaneous complaints of sleep disorders from the parents. After their children were recruited, parents filled a sleep diary for 2 weeks and the Child Sleep Habit Questionnaire (CSHQ); children were then recorded for 2 consecutive nights in a sleep laboratory. Sleep stages of night 2 were scored according to Rechtschaffen and Kales (1968) using 20 sec. epochs. Stage 2 sleep spindles and K-complexes were visually scored on bilateral prefrontal and central electrodes; REM sleep rapid eye movements were also scored. Variables were log transformed when abnormally distributed. Groups were compared using t-tests for independent samples.

Results: The CSHQ showed no significant group differences. Sleep diaries showed a longer sleep latency in autistic children (43.6±39.0 minutes vs. 17.2±17.5 minutes, p=.037). Polysomnographically recorded sleep latency was longer in autistic children (33.0±8.3 minutes vs. 14.4±4.6 minutes, p=.023), the duration of stages 3 and 4 (slow-wave sleep: SWS) was shorter (18.2±3.2 % vs 23.6±5.7 %; p=.009) but total sleep time was similar (539.7±54.3 vs. 560.8±60.2; p=.94). Sleep spindle density (per hour of Stage 2) was similar in both groups at central electrodes and Fp1 but it was lower at Fp2 (119.2±97.7 vs. 225.5±122.2, p=.03). The density of K-complexes was lower at the four electrodes (.0001<p< .01). REM sleep parameters (latency, duration, distribution, eye movement density) were not different between groups.

Conclusions: These results show that autistic children without subjectively reported sleep difficulties according to the CSHQ show signs of poor sleep on sleep diaries and polysomnography. Sleep diaries disclosed longer sleep latencies. Most polysomnographic differences were in nonREM sleep, raising the hypothesis of a difficulty for autistics to synchronize their cortical activity, possibly leading to impaired cortical sleep protective mechanisms such as low densities of sleep spindles and K-complexes.

**138.047 47** Stage 2 Sleep and Intelligence Measures in Autistic Children. S. Tessier[1], A. Lambert[1], E. Chevrier[1], P. B. Scherzer[2], I. Soulières[3], L. Mottron[4] and R. Godbout*[5], (1)*Sleep Laboratory & Clinic, Hop. Riviere-des-Prairies*, (2)*Universite du Quebec a Montreal*, (3)*University of Quebec in Montreal*, (4)*Centre de Recherche de l'Institut Universitaire de Santé Mentale de Montréal*, (5)*Sleep Laboratory & Clinic, Hop. Riviere-des-Prairies, Universite de Montreal*

Background: Sleep spindles are EEG waves thought to reflect sleep protective mechanisms that inhibit the processing of potentially arousing stimuli. Studies showed that sleep spindle activity correlate with IQ scores in typically developing individuals. Sleep spindles are diminished in children and adults with autism compared to typically developing individuals.

Objectives: We investigated whether the relationship between IQ scores and sleep spindles activity differed in children with autism

Methods: Thirteen boys with high functioning autism (HFA: 10.2 ± 2.1 years old) and 13 comparison children (COM: 10.2 ± 2.0 years old) were recorded for two consecutive nights. They completed the WISC-III in the morning after night 2. The absolute number of sleep spindles, spindle index (number of spindles /hour) and sigma EEG power (slow: 12-13 Hz, fast 13.25-15.75 Hz) were recorded and computed from frontal (Fp1, Fp2)

and central (C3, C4) electrodes during Stage 2 sleep. Results from the two groups were compared using Student t-tests and Mann-Whitney U-tests. Correlations between EEG measures and IQ were tested using Pearson's rho (alpha=.05).

Results: There were no significant group differences on IQ (HFA: Global =105.2±18.7, Performance=106.2±13.0, Verbal=103.8±22.3; COM: 115.8±10.3, 114.1±12.1, and 115.1±12.8, respectively). Spindle number and density were lower in the HFA group than in the COM group at the Fp2 recording site (669.7±467.3 and 126.8±87.1 vs. 1018.8±466.4 and 216.2±121.2). The HFA group showed a **negative** correlation between spindle density at the C3 recording site in the first quarter of the night and the WISC global (r=-0.52) and verbal (r=-0.62) IQ scales. Sigma power was significantly lower in the HFA than the COM group for C3 and C4 recording sites in the last quarter of the night (HFA: C3=0.925±0.096, C4=0.650±0.226; COM: C3=1.06±0.18, C4=0.888±0.301). The COM group showed a **positive** correlation between fast Sigma activity at the C4 recording site in the last quarter of the night and global IQ (r=0.592). There were no significant correlation between IQ and Sigma activity in the HFA group.

Conclusions: These findings indicate that the relationship between sleep EEG and IQ is different in autistic and typically developing children, both with normal IQ scores. These differences are in terms of scalp location (frontal vs. more posterior), EEG markers (spindle EEG wave density vs. Sigma activity spectral power), time of night (early vs. late night) and, more strikingly, direction of correlation (positive in COM, negative in HFA). Further analyses with more scalp locations and spectral analysis of sleep spindle are under way in order to better characterize the sleep EEG/IQ relationship.

**138.048 48** The Neural Basis for Atypical Pupillary Light Response in Autism Spectrum Disorder. S. E. Christ*, A. J. Moffitt, C. Daluwatte, M. H. Price, J. H. Miles and G. Yao, *University of Missouri*

Background: Pupillary light reflex (PLR) refers to the involuntary pupillary restriction that is induced by a luminance change. Recent studies (e.g., Daluwatte et al., 2013; Fan et al., 2009) have documented atypical PLR (i.e., longer PLR latency, smaller constriction amplitude, and lower constriction velocity) in individuals with Autism Spectrum Disorder (ASD). The primary neurological pathway subserving the PLR response is well-established and comprises the retina, pretectal nucleus, Edinger-Westphal nucleus, and ciliary ganglion (Lowenstein & Loewenfeld, 1950). There is also evidence, however, of tertiary cortical and cerebellar contributions to PLR (e.g., Tsukahara et al., 1973). Within this context, the neural locus of ASD-related abnormalities in PLR remains unclear.

Objectives: Functional magnetic resonance imaging (fMRI) was used to examine the neural disruption(s) that contribute to atypical PLR in ASD.

Methods: A sample of 25 individuals with ASD (mean age = 16.0 years) and a demographically-matched comparison group of 19 neurologically intact individuals without ASD (mean age = 16.0 years) participated. Scans were obtained on a 3T Siemens Trio scanner with a standard 8-channel head coil. Stimuli were displayed using an LCD projector, and pupillary responses were recorded using a MRI-compatible ASL long range optic eye tracking system. Participants performed a passive viewing task in which they were shown a series of red-filtered, emotionally-neutral images (e.g., landscapes) that changed every 5 s to maintain the interest of the participant. Every 20 s, the participant was presented a green-filtered light stimulus superimposed over the current image for 100 ms. The light stimulus was designed to induce PLR. For each participant, PLR and neural responses were recorded for a total of 96 light stimulus trials. Trials were presented over the course of 8 functional MRI runs, each of which lasted approximately 4 1/2 minutes.

Results: As anticipated, both groups showed robust PLR-related activation in primary visual sensory areas including lateral geniculate nucleus [$F(1,40) = 16.3$, $p < .0005$] and striate cortex [$F(1,40) = 17.8$, $p < .0005$]. PLR-related activation was also observed in association areas including superior parietal cortex [$F(1,40) = 17.4$, $p < .0005$] and right lateral prefrontal cortex [$F(1,40) = 9.0$, $p < .05$]. Most importantly, group differences in PLR-related activation were evident in the cerebellum as well as anterior insula and superior frontal gyrus, [$F(1,40) > 20$, $p < .00005$ in all instances].

Conclusions: These results are consistent with the hypothesis that prolonged PLR latency observed in individuals with ASD is associated with cerebellar and prefrontal dysfunction.

**138.049 49** The Neural Correlates of Perceptual Closure in Adults and Elderly with Autism. P. C. M. Koolschijn* and H. M. Geurts, *University of Amsterdam*

**Background:**
Perceptual closure refers to the ability to form a global and coherent perceptual representation on the basis of few details. A classical example is provided by two-tone (black and white) images of human faces (Mooney faces). In a Mooney image, the local features become too ambiguous to be recognized individually, and must be disambiguated based on their context within a global configuration. Mooney faces have been used to investigate various aspects of intact and impaired face processing. Given that autism is typically associated with a detail-oriented visual processing style, the neural mechanisms underlying perceptual closure may be different in patients with autism spectrum disorders (ASD).

**Objectives**:
Examine the neural mechanisms underlying perceptual closure in adults and elderly with ASD.

**Methods**:
Using 3T event-related fMRI we measured BOLD-signal changes in 27 patients with ASD (31-76yrs) to investigate how the brain forms perceptual decisions about complex visual forms. One hundred upright faces and 100 visually similar non-face images were shown for 200ms in a random sequence. To identify closure-related activity contrasts of correctly identified faces minus non-faces were computed. Post-scanning tests included a self-paced shortened version of the same perceptual closure task to examine the overall ability to recognize face stimuli. To assess global-local interference processing, a Navon hierarchical figures test (large "global" letters composed of smaller "local" letters) was administered.

**Results:**
*Behavior*
Preliminary data suggest that participants with ASD show significant reduced detection rates (M=65% vs 92%; p<.001), but not reaction times (p>.1) during the perception of Mooney faces compared to non-faces. Performance inside the scanner and the self-paced task outside the scanner was significantly different, such that performance on the self-paced task showed higher hit-rates for faces (M=79%; p<.01) and non-faces (M=96%; p<.01). Reaction time differed between faces and non-faces (1.6s vs 2.2s; p=.014). The average local-global precedence score (LGP; local RT- global RT) was 41.4ms (SD=199.2ms) suggesting that, overall, there was no significant local or global precedence effect for the group (i.e. LGP was not significantly different from zero; $t$=1.8, d.f.=26, $p$=.29). No significant associations were found between measures of the Navon task and the perceptual closure task performance.
*fMRI*
The fMRI data showed increased activation for faces relative to non-faces in the right fusiform face area (FFA), bilateral inferior frontal gyri, bilateral parietal lobule, left amygdala and right angular gyrus and insula (FDR corrected: p<.05; >10 contiguous voxels). No age-related effects were found for behavioral and neuroimaging data.

**Conclusions:**
The behavioral data suggest that face recognition is more dependent on holistic processing than non-face recognition or global-local interference processing. This finding is further strengthened by the large difference in detection rates in the self-paced task. The fMRI data showed typical responses in the FFA and inferior frontal gyri consistent with other recent studies demonstrating increased activation for faces compared to non-faces in autism. Overall, these findings suggest a specific face recognition deficit in adults and elderly with ASD independent of age. While informative, future analyses will include a matched healthy control group to elucidate whether these results are specific for ASD.

**138.050 50** The Role of Sustained Attention in the Association Between Dual Pathways and Language Function in Youths with High-Functioning Autism. S. S. F. Gau*[1], Y. C. Lo[2] and W. Y. I. Tseng[2], (1)*National Taiwan University Hospital and College of Medicine*, (2)*National Taiwan University College of Medicine*

Background: Language-communication deficit is one of the three core symptoms of autism. Our prior investigation found altered structure-function relations in autism suggest involvement of the dorsal (including arcuate fasciculus and superior longitudinal fasciculus Ⅲ) and ventral pathways (including inferior frontal-occipital

fasciculus and inferior longitudinal fasciculus) in compensating for the deficient semantic processing found in autism. In addition, literature documents the relationship between attention performance and language function. We hypothesized that the dual pathways in autism may work as a different mechanism compared to neurotypicals.

Objectives: The current study further investigates the role of attention performance in the association between dual pathways and language function.

Methods: Forty right-handed male youths with HFA and 40 matched neurotypical participants, aged 8 to 21, were assessed by the psychiatric interview (ADI-R and K-SADS-E) with their parents, intelligence test, the Conner's Continuous Performance Test (CCPT) and diffusion spectrum imaging (DSI). Images were acquired on a 3T MRI system with a 32-channel head coil (Tim Trio, Siemens, Erlangen, Germany). DSI tractography was reconstructed using a streamline-based algorithm adapted for DSI data and the targeted tracts were selected by expert-monitored multiple regions of interest (ROIs). ROIs for reconstructing the dual pathways followed the description by Saur *et al.* (Saur *et al.*, 2008). To select ROIs of each targeted tract objectively, we used MARINA software to define cortical regions as ROIs on the MNI template. For the dorsal pathway, two ROIs were identified, specifically, one at the left opercular part of inferior frontal gyrus (BA 44/46) and the other at the left superior temperal gyrus (BA 22). For the ventral pathway, the left orbital part of IFG (BA 47), left middle temporal gyrus (BA 21) and left fusiform gyrus (BA 37) were identified. Generalized fractional anisotropy values were computed along individual targeted fiber tracts to investigate alterations in microstructure integrity.

Results: We found that youths with HFA significantly scored lower in verbal IQ (106 vs 113) and verbal comprehension index (VCI, 107 vs 113) than neurotypicals without difference in performance IQ (106 vs. 109). Youths with HFA had significantly lower GFA of the left ventral pathway than neurotypicals. However, left-greater-than-right asymmetry of dual pathways was absent in HFA youths. Lateralization index of the dorsal pathway was positively correlated with Verbal IQ in neurotypicals (r=0.321, p=0.046). There were significant correlations between sustained attention and vigilance domains of the CCPT measures and GFA of right dorsal pathways as well as GFA of left ventral pathways (vigilance only) in HFA youths. Moreover, negative correlations between sustained attention and Verbal IQ/VCI in HFA youths (r=-0.420, p=0.008; r=-0.341, p=0.033, respectively).

Conclusions: Our results suggest the altered white matter alterations and less leftward lateralization of dual pathways in HFA and dual pathways involved not only language but also attention in HFA. Moreover, attention performance (particularly sustained attention) may mediate the prediction of microstructured integrity of dual pathway to language function. Taken together, the roles of the dual pathways may differ between HFA youths and neurotypicals.

**138.051 51** Wanting It Too Much: The Unexpected Effect of Social Motivation on Emotion Recognition. H. D. Garman*, C. Spaulding and M. D. Lerner, *Stony Brook University*

Background: Deficits in facial emotion recognition (FER) have sometimes been found to be key challenges in autism spectrum disorders (ASD; Harms et al., 2010), yet the source and nature of these deficits remain unknown. The social motivation theory posits that deficits in social 'wanting' may be one predictor of FER ability in individuals with ASD (Dawson et al., 2005; Kohls et al., 2012), though this relation has not been examined. Additionally, individuals with ASD show categorical delays in early electrophysiological processing of faces (specifically latency of N170 ERPs; McPartland et al., 2011). Moreover, these delays correlate with impairments in FER, as evidenced by slower latencies in N170, especially with subtle (Wong et al., 2012) and adult faces (Lerner et al., 2013). Consequently, this ERP may provide insight into the neurocognitive processes facilitating a link between FER and social motivation.

Objectives: The aim of this study is to determine the relationships between social motivation, FER and the N170. We hypothesize that social motivation will be positively correlated with better FER performance and this correlation will be driven by low intensity and adult faces. Furthermore, social motivation will be positively correlated with faster N170 latencies and N170 latencies will moderate the relationship between social motivation and FER performance.

Methods: Participants included 34 well-characterized adolescents (26 male; $M_{age}$ = 13.07, SD = 2.07) with ASD with intact cognitive ability. Parents completed the Dimensions of Mastery Questionnaire (DMQ), measuring social motivation. While, participants completed the Diagnostic Analysis of Nonverbal Accuracy-2 (DANVA-2), a well-established FER measure, ERP data, including the N170, were recorded.

Results: DMQ and DANVA-2 were significantly correlated (r = -.40, p = .016), indicating that greater social motivation predicted *poorer* emotion recognition. Post-hoc probing demonstrated that these effects were driven by the relationship between DMQ and low intensity (r = -.46, p = .003) and child faces (r = -.39, p = .011), and these results maintained after controlling for ASD severity (ADOS score) and IQ. N170 latency did not correlate with DMQ or overall DANVA-2, though it correlated with the DANVA-2 child faces subscale (r = .29, p = .05). To examine whether there is shared variance in the relations between DMQ, N170 latency, and DANVA-2 child faces relationships, a multiple regression was run predicting DANVA-2 child scores; this analysis suggested no reduction in either effect after control of the other, indicating two parallel pathways to emotion perception in child faces.

Conclusions: Contrary to our hypothesis, social motivation evinced a negative relationship with FER. These findings indicate that some individuals with ASD may be so highly socially motivated that they fail to attend to important (especially subtle and child peer-initiated) emotional cues in others. Thus, rather than being essential to adaptive outcomes in ASD (Kohls et al., 2012), social motivation may have important unanticipated consequences. Notably, while N170 latency revealed a modest relationship with FER, this effect appeared to be independent of the relationship with social motivation, suggesting that FER ability may be an equifinal and multifaceted construct in this population.

## 139 Brain Structure

**139.053 53** Measuring and Reducing Acoustic Noise in MRI Studies of Infants: A Review of Existing Guidelines and Development of New Methods. M. Valente*[1], S. Shultz[2], A. Klin[3] and W. Jones[3], (1)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*

***Background*** **:** Magnetic Resonance Imaging (MRI) is an important tool for charting brain development. This research initiative may provide critical insight into the neurodevelopmental processes associated with the emergence of ASD. Despite the promising potential of MRI, one major disadvantage is the intensity of acoustic noise that scanners generate while in operation. With noise levels reaching up to 120db, hearing protection is critical to ensure the comfort and safety of infant participants. Unfortunately, effectively reducing noise exposure in infant populations poses unique challenges that are not readily met by commercially-available hearing protection devices (HPDs). For instance, common HPDs, including earplugs, earmuffs, and headphones, do not have a mechanism to gauge if attenuation has been reduced during a session due to movement of the HPD. Instead, these HPDs rely on proper initial placement to facilitate noise reduction. In addition, few guidelines exist for what constitutes an acceptable level of noise in an MRI study of infants or how to reliably measure infants' acoustic environment. In the current study, we aim to attenuate the intensity of noise levels during MRI in order to accommodate infant participants.

***Objectives:*** The aims of this project are to: (1) review existing guidelines for sound measurement and attenuation in MRI studies of infants; (2) record accurate measurements of acoustic emissions from a Siemens 3T Tim Trio to determine the amount of sound attenuation necessary for a safe infant scan; and (3) create a HPD, specifically designed for infants, that provides sufficient sound attenuation and allows researchers to monitor the level of sound attenuation in real time, thereby ensuring that effectiveness is maintained throughout the scan session.

***Methods:*** Studies on acoustic emissions from MRIs, ANSI standards for measuring HPD effectiveness, and sound conduction pathways in the human body were reviewed. Acoustic emissions generated by the MRI and the effectiveness of a HPD designed for infants will be measured and tested in 1-to 9-month-olds (n=20).

***Results:*** Findings from the literature review guided the development of our framework for creating and measuring the effectiveness of a customized HPD for infants. The attenuation properties of our HPD will be tested outside the scanner by playing recordings of scanner sounds (MRI, DTI, and fMRI sequences to be used in infant studies) at reduced amplitudes (~60db). Attenuation will be measured with built-in MR-safe microphones that record sound pressure levels (SPL) outside each ear. The noise reduction (NR) scale will be used in recording these measurements with the transfer function of open ear (TFOE) correction to account for natural amplification by the pinna and ear canal. The microphones integrated into the HPD design will allow for continuous monitoring of sound attenuation during a MRI scan.

***Conclusions:*** This research demonstrates a first step towards the development of an HPD, custom-made for infants, that reduces scanner noise to a safe level and allows real-time monitoring of the effectiveness of the HPD throughout a scan session. Using the principles learned from the existing literature, our immediate next steps include completing the design and testing of this customized HPD.

**139.054 54** A 'Bottom-up' Approach to ASD: The Anatomy of Precision Grasping Deficits in ASD: Focus on a Newly Described Set of Fronto-Parietal Connections. A. Thompson*[1], M. Catani[1], F. Dell'Acqua[1], C. Ecker[1], G. M. McAlonan[2] and D. G. Murphy[1], (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Psychiatry, King's College London*

Background:

It is commonly reported that individuals with ASD have abnormalities in motor co-ordination (dyspraxia), and that these frequently precede clinical signs in ASD. This is of importance as fine motor skill such as precision grasping ability can be rapidly and objectively measured by clinicians. Furthermore, advanced neuroimaging methods based on diffusion imaging tractography give direct access to networks underlying sensory-motor integration. In this study we test the hypothesis that impaired precision grasping in ASD is associated with specific abnormalities of the connections between the primary motor (M1) and somatosensory (S1) cortices specialised in sensory-motor integration of the fingers.

Objectives:

To perform virtual *in vivo* dissections of the U-shaped connections between M1 and S1 and investigate whether white matter abnormalities correlate with performances in precision grasping in ASD.

Methods:

We included 120 individuals from the Autism Imaging Multicentre Study (MRC AIMS Consortium). Sixty right-handed adult male participants with ASD (above cut off on the Autism Diagnostic Interview-Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS)) and 60 age-matched controls (age 18-50, IQ > 70). The Purdue Pegboard Test was administered as a measure of precision grasping. Diffusion Tensor Imaging-Tractography (DTI) was used to compare, *in vivo*, the microstructural organization of the FPUTs bilaterally between subjects with ASD and healthy controls – as indexed by fractional anisotropy, mean diffusivity and perpendicular diffusivity.

Results:

The ASD group performed significantly less well on the Purdue Pegboard test in the right hand ($t=2.08$, $p = .040$) and both hands assembly measure ($t=3.98$, $p < .001$). Compared to healthy controls, individuals with ASD showed significantly greater mean diffusivity and perpendicular diffusivity and lower fractional anisotropy on both left and right FPUT ($p < 0.025$ in all cases). In the control group higher scores on the pegboard test correlated significantly with increased microstructure of the left-hemisphere FPUT (increased fractional anisotropy, decreased mean diffusivity and decreased perpendicular diffusivity). In the ASD group pegboard scores did not correlate with left FPUT structure, but did correlate significantly with increased microstructure of the right-hemisphere FPUT (increased fractional anisotropy, decreased mean diffusivity and decreased perpendicular diffusivity).

Conclusions:

We found that precision grasping impairment in ASD is associated with altered structure of the FPUTs. We found an association between Pegboard performance and the structure of the

left hemisphere tracts in the control group, which is in line with left-hemisphere dominance of praxis. We did not find this left-hemisphere association in ASD, and found an anomalous right-hemisphere association. This suggests the loss of neurotypical lateralization of sensory-motor integration for precision grasping in ASD. Precision grasping assessment may be a reliable proxy measure for assessing generalised brain abnormality in ASD.

**139.055 55** Cerebellar Grey Matter and Lobular Measures Correlate with Core Autism Symptoms. A. M. D'Mello*[1], D. Crocetti[2], S. H. Mostofsky[2] and C. J. Stoodley[1], (1)*American University*, (2)*Kennedy Krieger Institute*

Background: Anatomical differences in the cerebellum are among the most consistent post-mortem findings in autism spectrum disorder (ASD). Previous structural neuroimaging findings show grey matter (GM) decreases in lobules VII (Crus I), VIII and IX, VIII of the cerebellum. Similarly, individuals with autism show reduced activation in right anterior cerebellum, Crus I, and Crus II during a variety of motor, executive functioning and language tasks. In clinical studies, malformations and acquired lesions in the cerebellum can result in ASD symptomology. In particular, lesions affecting the posterior cerebellum can result in language difficulties, affective dysfunction, and problems in executive functioning – symptoms relevant to ASD. Recent evidence also suggests that there are functional subregions within the human cerebellum for sensorimotor and cognitive processing; the anterior lobe connects to primary sensorimotor areas of the cerebral cortex, whereas the posterior lobe connects to prefrontal and parietal regions. This provides an important framework in interpreting cerebellar findings in ASD.

Objectives: We investigated cerebellar regional grey matter (GM) and volumetric measurements of the cerebellar lobules in ASD children compared to typically-developing (TD) children, and examined the relationship between cerebellar structure and core ASD symptoms.

Methods: Voxel-based morphometry (VBM) was used to compare whole-brain GM in 35 ASD and 35 TD children (mean age 10.4 ±1.6 years; range 8-13 yrs). The cerebellar SUIT atlas was used to compute volumetric measurements of individual cerebellar lobules. Correlations were calculated between scores on the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview (ADI) and the VBM and volumetric data.

Results: VBM revealed reduced GM in ASD children bilaterally in cerebellar lobule VII (Crus I/II). More impaired scores on the ADOS Social Interaction subscale correlated with reduced GM in seven cerebellar clusters, including right Crus I/II. More impaired scores on the ADOS Social-Communication subscale correlated with reduced GM clusters in right Crus I/II and VIIIA/VIIIB. Poorer ADOS Stereotyped Behaviors & Restricted Interests scores correlated with reduced GM in regions of right Crus I/II. In addition, more impaired scores on the ADI Social Interaction and Restrictive, Repetitive & Stereotyped Behaviors subscales correlated with reduced GM in a cluster in the anterior cerebellum. Consistent with the VBM findings, the SUIT volumetric analysis revealed smaller right Crus I in the ASD group. Volumetric analyses also revealed larger vermis lobules VIIIA and VIIIB in children with ASD. Smaller vermis VI volume correlated with more impaired ADOS Social Interaction and ADI Communication scores. Poorer ADOS Stereotyped Behaviors & Restricted Interests scores were associated with smaller volumes in lobule VIIIB bilaterally. Larger vermis VIIB and VIIIA volumes were associated with worse ADI Restrictive, Repetitive & Stereotyped Behaviors.

Conclusions: Using two analytic approaches, we showed reduced cerebellar Crus I/II GM in ASD, a region which connects to prefrontal and parietal association areas. Importantly, cerebellar GM volume and lobule volumes significantly correlated with ASD severity, providing further evidence of a role for the cerebellum in ASD etiology.

**139.056 56** Amygdala and Hippocampal Morphology in Youth with High Functioning Autism Spectrum Disorders. R. A. Vasa*[1], X. Tang[2], D. Crocetti[1], T. Brown[2], T. Ratnanather[2], M. I. Miller[2] and S. H. Mostofsky[1], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins University*

Background: The amygdala and hippocampus are two medial temporal lobe regions implicated in emotion processing and psychopathology, and are hypothesized to play a role in the neuropathology of autism spectrum disorder. Controversy exists, however, regarding the nature of these abnormalities in ASD. For example, some data indicate enlarged amygdala volumes in childhood (Schumann et al., 2004), whereas other data

indicate that amygdala volumes normalize by late childhood (Barnea-Goraly et al., 2013). Hippocampal data are also inconsistent and show enlarged (Sparks et al., 2002), reduced (Aylward et al., 1999) or no change (Piven et al., 1998; Haznedar et al., 2000) in volumes. These discrepant findings may be attributed to sample heterogeneity as well as limitations in imaging methodologies used to examine amygdala and hippocampus volumes. A fine grain analysis of these brain structures is therefore warranted in order to better delineate neuropathology. The current study uses large deformation diffeomorphic metric mapping (LDDMM), a powerful brain mapping tool, to examine shape abnormalities in the amygdala and hippocampus in youth with ASD.

Objectives: 1) To examine differences in amygdala and hippocampus morphology (shape and volume) between children with high functioning autism (HFA) and typically developing children; 2) To determine if localized differences in amygdala and hippocampal morphology (shape and volume) in the HFA group are associated with clinical symptoms.

Methods: High resolution T1 scans from 82 subjects with high functioning autism or Asperger's Disorder (mean age = 10.5 years, 85 % male, IQ > 80), along with 190 typically developing children (mean age =10.3, 69% male, IQ > 80) were examined. All children underwent a comprehensive assessment that included administration of the Diagnostic Interview for Children and Adolescents (DICA), Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview (ADI-R), dimensional measures of psychopathology, and an IQ test. Amygdala and hippocampal volumes will be manually delineated on a subset of the sample in order to create the multiple atlas set, which will then be used to segment the two structures of interest. For each structure, LDDMM-surface mapping will be used to transfer a common template surface onto a triangulated surface contouring the amygdala and hippocampus for each subject. Deformation maps will then be computed and used for examining group differences in local shape measurements as well as correlations between shape and clinical measures.

Results: Investigators of this study have extensive experience in conducting morphological analyses of brain structures (e.g., Qui et al., 2010). Delineation of amygdala and hippocampus shapes and volumes are currently underway. Data analyses will examine the effect of diagnoses on morphological variables. Correlations will be performed to examine for associations between brain morphology and behavioral measures, including ASD specific symptom domains, an ADOS based measure of autism symptom severity, and measures of anxiety.

Conclusions: This is one of the first, and potentially the largest, structural MRI study examining amygdala and hippocampal morphology in a relatively homogeneous group of children with ASD. Findings may provide insights into abnormal neuronal organization within these structures and their relation to the clinical phenotype of ASD.

**139.057 57** Clinical Relevance of MRI Scanning in a Sample of 101 ASD Individuals: Evidences from EEG and MRI Findings. F. Piras*[1], M. Carta[1], D. Serra[1], G. Bitti[1], M. T. Peltz[1], S. Secci[1], R. Fadda[2] and G. S. Doneddu[1], (1)*Azienda Ospedaliera Brotzu*, (2)*University of Cagliari*

Background: EEG abnormalities are much frequent in ASD subjects, especially with Intellectual Disability(ID) (Volkmar and Nelson, 1990). On the contrary, the clinical relevance of MR scanning in individual with ASD is quite controversial. Moreover, little is still known about the relation between ID and MRI abnormalities in ASD. Brambilla et al. (2003) reviewed the structural MRI studies published from 1966 to May 2003: the most replicated abnormalities in ASD were increased total brain, parieto-temporal lobe, and cerebellar hemisphere volumes. Moreover, recent findings indicated that the size of amygdala, hippocampus, and corpus callosum(mkght be abnormal. Furthermore, ASD individuals might be characterized by abnormalities in neural netwozk involving fronto-temporo-parietal cortex, limbic system, and cerebellum. However, Filipek (1999) found that the prevalence of lesions detected by MRI in children with ASD has been reported to be similar to typically devmloping controls. Recently, a new study demonstrated structural atypicalities in the temporal cortex and adjacent cortical structures, associated with EEG abnormalities ( Ozlem et al.,2009). Thus, the debate on the clinical relevance of MR scanning in children with ASD is

still open. New studies are necessary with sizeable and well-characterized groups of ASD individuals. Moreover, the co-occurrence of MRI and EEG abnormalities and ID might be of interest.

Objectives: We aimed to evaluate the MRI findings and EEG and their relation with ID in a large group of individuals with non-syndromic Autism Spectrum Disorder (ASD).

Methods: MRI inspection of 101 individuals with non-syndromic ASD (75M; age range: 2yrs 8 months- 23yrs and 8 moths; mean= 9 yrs 10 months; SD=51) was performed under pharmacological sedation. All met the DSM-5, ADOS and ADI –R criteria for autism. All MRI scans were acquired with a 1.5-T Signa GE (DW1,FSE T1, FSE T2, 3-DT1-FSPGR, Gd ev). EEG investigations were recorded according to the 10–20 system. The EEG was performed during sleep and it lasted1 hour. Unless the sleep was spontaneous, we used melatonin mg 5 per dose. All patients were evaluated for cognitive development with one of the following scales: Griffith Scales, Wechsler Intelligence Scale for Patients-Revised or Leiter-R.

Results: The results indicated that 46/101 patients (45%) had abnormal EEG recordings. MRI abnormalities were detected in 47/101 patients (46%). The most frequent MRI abnormalities were bilateral periventricular leukomalacia 15/47 (32%), malformations of the brain 12/47 (25%), and mild cortical atrophy 10/47 (21%). 25/47 (53%) had abnormal EEG recordings together with abnormal MRI scans. ID was detected in 69/101 patients (68%). 31 of the 69 patients with ID (44%) had abnormal EEG recordings while 28/69 had abnormal MRI (40%). 15 of the 69 patients with ID (21% ) had abnormal EEG recordings and had abnormal MRI scans.

Conclusions: The results highlight the clinical relevance of MRI in ASD evaluation, especially in patients with EEG abnormalities and in the ones with ID. The co-occurrence of EEG abnormalities, ID and MRI abnormalities is present in a considerable percentage of these patients and therefore needs to be specifically investigated.

**139.058 58** An MRI Investigation of Neuroanatomical Differences in High Functioning Adults with Autism Spectrum Disorder Using Non-Parametric Cluster Based Statistics. D. S. Andrews*[1], E. Daly[1], J. Horder[1], M. A. Mendez[1], V. Giampietro[2], M. Brammer[2], C. E. Wilson[1], N. Gillan[1], C. Ecker[1] and D. G. Murphy[1], (1)*Institute of Psychiatry, King's College London*, (2)*Centre for Neuroimaging Sciences, King's College London*

Background: Voxel-based morphometry (VBM) is a statistical method for identifying regional differences in grey (GM) and white (WM) volumes. VBM investigations of autism spectrum disorder (ASD) have often been confounded by grouping individuals across different bands of the spectrum, periods of development, and/or comparison to inappropriately matched controls with regards to age and intellectual ability. Further more these studies commonly rely on parametric statistical methods and potentially overly stringent corrections for multiple comparisons. These methodological issues all potentially serve to conceal elements of the larger pattern of neuroanatomical differences observed in ASD.

Objectives: This study sought to identify regional differences in GM and WM volumes between a homogenous group of ASD participants compared to matched typically developing controls using non-parametric cluster based VBM. Correlations between GM volumes and number of observed ASD symptoms were also investigated.

Methods: Group comparisons of GM and WM volumes were conducted between 21 adult males with ASD (Age: 32 ± 8.87, IQ: 116 ± 13.88) and 21 typically developing controls (Age: 32 ± 9.76, IQ: 119 ± 8.42) matched for age and general intelligence. All ASD participants were diagnosed according to the *International Statistical Classification of Diseases, 10th Revision (ICD-10)* and were categorized as high functioning (IQ>80). Diagnosis was confirmed using the Autism Diagnostic Interview-Revised (ADI-R). Current symptoms were assessed using the Autism Diagnostic Observation Scale (ADOS). High-resolution T1 anatomical magnetic resonance images (MRI) were collected and segmented using VBM methods with Diffeomorphic Anatomical Registration using Exponentiated Lie algebra (DARTEL). Non-parametric cluster level statistical analysis using X-Brain Activation Mapping (XBAM v4.1) was performed to identify regional differences in GM and WM volumes, as well as correlations between GM volumes and ADI-R and ADOS symptom scores.

Results: Regional differences in the neuroanatomy of ASD participants compared to controls were revealed in the form of spatially distributed

significant clusters (permutation test *P*=.001) of GM and WM volumetric increases. GM increases encompassed several regions including the orbitofrontal and dorsolateral prefrontal cortices, superior temporal gryus, posterior parietal cortex, primary visual areas, fusiform gyrus and cerebellum. Spatially distributed WM abnormalities were identified across the brain including tracts that connect associative areas, namely the longitudinal facsiculus and corpus callosum. GM regions of the prefrontal cortex were also found to significantly correlate (permutation test *P*=.002) with ADI-R social scores.

Conclusions: Previous VBM studies in ASD have reported several contradictory findings. Cluster based non-parametric VBM methods allow for more sensitive identification of GM and WM volume differences in ASD. Furthermore, the recruitment of a homogenous group of ASD participants and appropriately matched controls serves to limit potential confounds. The current study identified significant distributed GM and WM volume increases across several brain regions known to mediate behaviors associated with ASD. By measuring tissue volume alone, VBM methods are inherently limited. Techniques such as surface-based morphometry (SBM) and diffusion tensor imaging (DTI) can aid in better defining the neuro-abnormalities present in ASD and provide valuable clues as to the underlying developmental processes potentially responsible for observed deficits in the disorder.

**139.059 59** Correlation Between Cerebellar White Neuroanatomy and a Motor Coordination Task in Autism Spectrum Disorder. R. H. Wichers*, E. Daly, M. AIMS, D. G. Murphy and C. Ecker, *Institute of Psychiatry, King's College London*

**Background:**
Structural neuroimaging studies suggest that Autism Spectrum Disorder (ASD) is accompanied by neuroanatomical differences in the cerebellum. For example, it has been shown that total cerebellar volume is significantly reduced in ASD (Hallahan et al., 2009). Also, a reduction in total cerebellar white matter volume in ASD has been observed (McAlonan et al., 2002).
However, most prior studies were based on measures of cerebellar volume, which is a neuroanatomical highly unspecific feature as it is computed as a product of cortical thickness and surface area. Also, most studies investigated the cerebellum globally (e.g. total cerebellar volume) rather than locally (i.e. different cerebellar sub regions). In addition, it is currently unknown how neuroanatomical cerebellar differences mediate specific autistic symptoms such as impaired motor control and coordination.

**Objectives:**
Here we aim to establish neuroanatomical differences in the cerebellum between individuals with ASD and controls using a spatially unbiased, surface-based approach based on the cerebellar white matter, and to correlate distinct morphometric features with autistic symptoms.

**Methods:**
We included 75 male adults, 38 diagnosed with ASD and 37 healthy controls who did not differ significantly in mean age and full scale IQ (respectively 26 + 7 years and 110 + 14; and 28 + 6 years and 114 + 14). The FreeSurfer image analysis suite was used to derive 3D models of the cerebellar white matter surface in each $T_1$-weighted image. Initially, we examined between-group differences in total cerebellar white matter volume. At each cerebellar vertex (i.e. point on the surface), we also examined between-group differences in curvature (C), cortical folding (i.e. sulcal depth) (SD) and surface area (SA) using an exploratory vertex-level threshold of $P < .05$ (uncorrected). Furthermore, correlations between distinct neuroanatomical features and performance in the Purdue Pegboard test were examined at each cerebellar vertex using a general linear model (GLM) with a main effect of group, a main effect of task performance, and their interaction. A t-test for independent samples was used to compare task performance between groups.

**Results:**
There were no significant differences in total cerebellar white matter volume between individuals with ASD and controls (p=0.076). However, we observed significant between-group differences in geometric features of the cerebellar white matter including curvature, sulcal depth and surface area, which occurred predominantly in cerebellar hemisphere lobule V and VI ($p<0.05$, uncorrected). Individuals with ASD performed significantly worse in the Perdue Pegboard test than controls (t=3.578, p=0.001). Last, we found a significant association between morphometric measures and general task performance in cerebellar hemisphere lobules IV, V, VI and VII, where we also found a significant interaction

between performance measures and diagnostic category.

**Conclusions:**
In summary, our data suggests that individuals with ASD have significant differences in the geometry of their cerebellar white matter, which may contribute to impairments in motor coordination. Our study therefore provided an important first step into describing cerebellar white matter neuroanatomy using a surface-based approach in individuals with ASD, which may aid future investigations into the specific underlying neural mechanisms of ASD.

**139.060 60** Manual Motor Performance Related to Autistic Traits, Daily Living Skills, and White Matter Microstructure in Autism Spectrum Disorder. B. G. Travers*[1], E. D. Bigler[2], D. P. Tromp[3], N. Adluru[4], D. J. Destiche[4], M. D. Prigge[2], A. Froehlich[2], N. Lange[5], A. Alexander[3] and J. E. Lainhart[6], (1)*Waisman Center University of Wisconsin-Madison*, (2)*University of Utah*, (3)*University of Wisconsin*, (4)*University of Wisconsin-Madison*, (5)*McLean Hospital*, (6)*Waisman Center, University of Wisconsin-Madison*

Background: Mounting evidence suggests that individuals with Autism Spectrum Disorder (ASD) exhibit poorer motor skills and that these poorer motor skills may be related to more severe core ASD symptomatology and poorer adaptive functioning (Hilton et al., 2007; MacDonald, Lord, & Ulrich, 2013; Radonovich et al., 2013;Travers et al., 2013). However, the causal nature of this relation is unknown. Because motor function, social communication, and adaptive functions likely require an integration of information across the entire brain, it is possible that decreased white matter microstructural integrity is a third variable that could be affecting both motor skills and core ASD symptoms.

Objectives: 1) To examine the relation between manual motor performance (i.e., grip strength and finger tapping speed) and ASD traits/adaptive functioning, while controlling for age and IQ. 2) To examine whether the relation between motor function and ASD symptomatology/adaptive functions was mediated by whole-brain white matter microstructural integrity, as measured by Diffusion Tensor Imaging (DTI).

Methods: Seventy males with ASD and 41 males with typical development between the ages of 5 and 33 years participated in this study (Time 1 data of a broader longitudinal study). Participants completed bimanual measures of grip strength and finger tapping speed. The Social Responsiveness Scale measured autistic traits, and the Vineland Adaptive Behavior Scale measured adaptive functioning. Participants completed a DTI scan (12 directions, $b$ = 1000 s/mm$^2$, one b0 image, 60 contiguous axial slices, matrix= 128 x 128, FOV = 256mm, resolution= 2 x 2 x 2.5 mm, averages = 4, TR = 7000 ms, TE = 84 ms). Average whole-brain white matter fractional anisotropy (FA) was calculated across the deep white matter tracts. Independent-samples t-tests examined group differences in manual motor performance. Partial correlations examined the relation among manual motor performance, ASD traits/adaptive functioning, and whole brain FA, while controlling for age and IQ.

Results: The ASD group demonstrated weaker grip strength, $t(109) = 2.14$, $p = .04$, and slower finger tapping, $t(109)=2.03$, $p=.046$, compared to the typically developing group. After controlling for age and IQ, weaker grip strength, $r=-.20$, $p<.05$, and slower finger tapping, $r=-.20$, $p<.05$, were found to relate to more severe autistic traits across the combined sample. Similarly, weaker grip strength was found to relate to more difficulty with daily living skills, $r=+.28$, $p=.007$. Grip strength, $r=+.23$, $p=.01$, and finger tapping speed, $r=+.35$, $p<.001$, were also found to relate to whole-brain white matter FA across both groups combined. However, there were no reliable relations between whole-brain white matter FA and autistic traits or daily living skills ($p$'s>.48).

Conclusions: The present results suggest that manual motor performance is associated with autistic traits, daily living skills, and white-matter microstructural integrity in individuals with ASD. However, after controlling for age and IQ, white matter microstructure was not related to autistic traits or daily living skills, which suggests that whole-brain white matter microstructure is not a mediating variable between motor function and autism symptomatology.

**139.061 61** A Twin Study of Autism Spectrum Disorder and MRI-Brain Incidental Findings. J. C. Monterrey*, J. Phillips, S. Cleveland, J. F. Hallmayer and A. Y. Hardan, *Stanford University School of Medicine*

Background: Recent anatomic MRI-brain studies suggest the prevalence of asymptomatic "incidental" findings in autism spectrum disorder (ASD) is similar to that of typically developing

controls. However, given the causes of ASD likely combine genetic and environmental factors, a study design using twins with ASD would facilitate controlling for genetic and environmental biases. To date, such a twin model has not been used to study incidental MRI-brain findings in ASD.

Objectives: To use multi-modal high-resolution 3T MRI to assess the prevalence of incidental findings in monozygotic (MZ) and dizygotic (DZ) twins with ASD, in comparison to typically developing control twins.

Methods: MRI-brain scans of same-sex, ASD twins and typically developing twins between the ages of 6 and 15 years were obtained using a GE 3T scanner employing multiplanar T1 and T2 sequences. Incidental findings consisted of anatomic variants agreed upon by two neuroradiologists blinded to diagnosis.

Results: MRI data were available from 16 twin pairs (8 MZ; 8DZ) where both have ASD, 12 twin pairs (3 MZ; 9 DZ) where only one twin has ASD, and 17 control twin pairs (6 MZ; 11 DZ) where neither twin has ASD. In total there were 44 subjects with ASD, 12 typically developing siblings of ASD twins, and 34 controls. No significant difference was found between prevalence rates in subjects with ASD, typically developing siblings of ASD twins, and typically developing control twins (73%, 83%, and 65%, respectively, chi-square= 1.61, p=0.4). McNemar's test for correlated proportions of twins with ASD and their typically developing twin siblings showed no association between ASD and incidental MRI-brain findings (OR 2.0, 95% CI: 0.18-22.1, p=0.5).

Conclusions: These preliminary findings are consistent with the available literature suggesting the absence of increased incidental findings associated with ASD. Studies with large sample size would have the statistical power to detect smaller effect sizes while appropriately controlling for genetic and environmental biases. Additionally, the examination of the specific type of incidental finding would also be interesting, but larger number of participants will be needed.

**139.062 62** Elevated Extra-Axial Cerebrospinal Fluid in Toddlers with Autism Spectrum Disorder. M. D. Shen*, C. W. Nordahl, D. D. Li, A. Lee, K. Angkustsiri, S. Ozonoff, S. J. Rogers and D. G. Amaral, *University of California Davis Medical Center*

Background: Extra-axial fluid is characterized by excessive cerebrospinal fluid in the subarachnoid space, particularly over the frontal lobes. We previously reported that infants who later developed autism spectrum disorder (ASD) had an elevated amount of extra-axial fluid at 6-9 months of age, which persisted and remained elevated through 24 months of age. The amount of extra-axial fluid in infancy was predictive of more severe ASD symptoms at the age of diagnosis. It is unknown whether excessive extra-axial fluid remains abnormally elevated beyond infancy and if its presence is associated with clinical or medical factors.

Objectives: The objectives of the current study was to replicate and extend these findings in a large, independent sample of toddlers with ASD and to identify clinical and medical factors associated with this brain anomaly. Our hypothesis was that toddlers with ASD would continue to show a persistent elevation of extra-axial cerebrospinal fluid, compared to age-matched typically developing control children (TD).

Methods: This study was conducted as part of a larger multidisciplinary study at the UC Davis MIND Institute aimed at identifying subtypes of ASD. The current sample included all children who had a successful structural MRI between 2-4 years of age (mean age 38.2 months, SD=6.46). The total sample included 277 children, 187 with ASD (153 male, 34 female) and 90 with TD (59 male, 31 female). High-resolution, T1-weighted structural MRI scans were acquired during sleep. Quantitative measurements of extra-axial fluid were obtained using an anatomical protocol developed by our laboratory and validated in a previous study. Medical examinations and medical history reviews were conducted by a board-certified developmental behavioral pediatrician. Behavioral and clinical assessments were conducted by a team of developmental and clinical psychologists.

Results: The ASD group had significantly greater volume of extra-axial cerebrospinal fluid compared to the TD group ($p<0.005$). This effect remained significant ($p=0.03$) when taking brain size into account, which indicated that extra-axial fluid was elevated out of proportion to overall brain volume. Both male and female toddlers with

ASD had greater extra-axial fluid compared to their typically developing counterparts.

Conclusions: This finding in a large, independent sample of toddlers with ASD suggests that elevated extra-axial cerebrospinal fluid is a structural brain anomaly that is detectable from infancy through early childhood in ASD. There is mounting evidence from neurobiological studies that persistently excessive cerebrospinal fluid in the subarachnoid space surrounding the developing brain alters the concentration of neural growth factors and potentially harmful metabolites that may have a pathological effect on normal brain development. We will examine several clinical and medical factors that might relate to the phenotypic variation of this brain anomaly in ASD, including ASD symptoms and cognitive function, prenatal and perinatal medical history, immune function, sleep problems, and other MRI brain measures.

**139.063 63** Relationship of 47,XYY Syndrome to ASD: Diffusion MRI Findings. L. Bloy*[1], T. P. Roberts[1] and J. Ross[2], (1)*Children's Hospital of Philadelphia*, (2)*Thomas Jefferson University*

Background: 47,XYY syndrome (XYY) occurs in ~0.1% of population-based males but is reported in 1% of males with autism spectrum disorders (ASD). Approximately 19-36% of males with XYY are reported to satisfy ASD diagnostic criteria. Diffusion tensor MRI (DTI) has implicated widespread differences in white matter (WM) microstructure in ASD versus TD children, with the predominant pattern of compromised WM of the frontal and temporal lobes. We compared these WM patterns of results in boys with XYY versus our previous findings in boys with idiopathic ASD (ASD-I).

Objectives: Using innovative neuroimaging biomarkers derived from DTI, we compared imaging results from boys with XYY with (XYY+ASD) and without ASD (XYY-ASD) versus age-matched typically developing boys (TD).

Methods: We performed ASD, cognitive, social function, and language evaluations and neuroimaging in 12 boys with karyotype-confirmed XYY (mean age 11.5±2.4y), using the Social Communications Questionnaire (SCQ), the Social Responsiveness Scale (SRS), and the Autism Diagnostic Interview-Revised (ADI-R). Verbal abilities were evaluated with the Differential Ability Scales (DAS). DTI results were acquired at Thomas Jefferson University on a Philips 3.0T MRI system and were used in combination with anatomical data to calculate mean diffusivity (MD) and anisotropy along select WM tracts from 12 XYY boys and 12 age-matched TD boys (mean age 11.6±1.8y). The DTIs were post-processed using the DTIstudio software and the tracks of the left arcuate fasciculus (AF) were determined by placing seed and target regions of interest in selected neuroanatomic locations.

Results: Six of the 12 XYY boys (50%) met ASD diagnostic criteria (XYY+ASD), based on thresholds of SCQ, SRS, and ADI-R. Comparison of the XYY+ASD versus XYY-ASD demonstrated that verbal function on the DAS verbal cluster was similar but one-word receptive language (ROWPVT) was relatively impaired in XYY+ASD and their behavioral outcomes on the Child Behavior Scale (CBCL) and SRS were worse. Both XYY groups differed from TD controls on these measures of language and social function, supporting group-wide findings of increased ASD risk in XYY, with differences in aspects of language, behavior, and social function between XYY+ASD and XYY-ASD. The averaged MD in the left AF for each group were: 8.18x10−4mm2/s (XYY+ASD), 7.94 x10−4mm2/s (XYY-ASD), and 7.85 x10−4mm2/s (TD). This 4.2 % increase in XYY+ASD is similar to the previously reported pattern seen in idiopathic ASD relative to TD controls, suggesting the sensitivity of this ASD marker within both the XYY as well as the general ASD-I populations.

Conclusions: These data support the group-wide findings of increased ASD risk in XYY and the overlap in imaging findings in XYY+ASD versus ASD-I. Elevated MD in the left hemisphere AF was observed in boys with XYY+ASD, suggesting a potential marker of ASD in XYY. The strong likelihood that increased Y-chromosome dosage and increased risk of ASD are significantly associated deserves further investigation and may identify a genetic component of the marked male predominance in ASD.

**139.064 64** Disproportionate Megalencephaly: A Clinically Meaningful Neurophenotype in Autism Spectrum Disorder. R. T. Johnson*[1], C. W. Nordahl[2], H. Ota[3], A. Kreutz[1], A. Lee[2], S. J. Rogers[2] and D. G. Amaral[2], (1)*MIND Institute and Department of Psychiatry and Behavioral Sciences, University of California Davis Medical Center*, (2)*University of California Davis Medical Center*, (3)*Showa University School of Medicine*

Background:

Increased head size was noted in the earliest descriptions of children with autism spectrum disorder (ASD). However, the prevalence of abnormal head size in ASD has been continually debated and uncertainty remains regarding any potential clinical implications. Recent findings suggest that children with ASD may exhibit accelerated growth in body length as well, but this has not routinely been accounted for in definitions of abnormal head size.

Objectives:

We sought to identify and characterize differences in gray and white matter of the brain in young boys with ASD who also exhibited disproportionate megalencephaly (ASD-DM).

Methods:

Children below the age of 5 with ASD as well as age-matched typically developing controls were recruited through the MIND Institute of the University of California Davis as part of the Autism Phenome Project. Diagnostic assessments were conducted by licensed clinical psychologists using the Autism Diagnostic Observation Schedule-Generic (ADOS-G) and the Autism Diagnostic Interview-Revised (ADI-R). Magnetic resonance imaging scans were collected during natural nocturnal sleep and included both T1 and diffusion-weighted sequences. The ASD-DM male subgroup was defined as individuals with a cerebral volume to height ratio 1.5 standard deviations above the typically developing mean.

Cortical thickness and surface area were measured in 4 lobes and 34 automatically parcellated brain regions in each hemisphere. Axial diffusivity, radial diffusivity, mean diffusivity, and fractional anisotropy were assessed along the length of 18 white matter tracts. Results in ASD-DM males were compared to results in all other males with ASD as well as to typically developing controls.

Results:

ASD-DM males exhibited cortical surface area alterations in the rostral middle frontal, fusiform, and rostral anterior cingulate regions as well as greater hemisphere asymmetry in frontal lobe surface area. Results from white matter analyses indicate diffusivity alterations principally in the anterior thalamic radiations, corticospinal tracts and uncinate fasciculus. Finally, behavioral assessments indicated the ASD-DM group performed more poorly on the social affect and communication and social interaction subscales of the ADOS compared to males with ASD and normal brain volumes.

Conclusions:

ASD-DM males display additional brain alterations not seen in other males with ASD. In conjunction with poorer scores on multiple behavioral measures, this suggests ASD-DM males may represent a more severely affected group of children within ASD. While additional characterization of ASD-DM males is necessary, identification of a subset of males with ASD who exhibit neurological and behavioral distinctions is an important starting point for delineation of specific autism phenotypes. Identification of subgroups within ASD will likely assist in the development of more effective therapies and treatments as well as inform efforts aimed at providing earlier diagnosis of ASD.

**139.065 65** Cerebral Morphometry in the Abide Data Set. M. Schaer*[1], C. J. Lynch[2] and V. Menon[1], (1)*Stanford University*, (2)*University of Georgetown*

Background:

Numerous published studies have delineated morphometric differences in the brain of children, adolescents and adults with autism spectrum disorders (ASD). However, most of these studies analyzed limited sample size, or specific populations in terms of age range, symptoms' severity or cognitive abilities, so that large-scale studies are needed to better understand how demographics and clinical profile influence the cerebral phenotype in ASD.

Objectives:

This study aims at exploiting the largest sample of subjects available to date to examine the structural brain differences in patients with ASD as compared to controls. Further, we sought to explore potential structural correlates of the varying symptoms' severity and cognitive level in autism.

Methods:

The ABIDE data set (http://fcon_1000.projects.nitrc.org/indi/abide/) comprises 1112 structural MRI, collected from 539 patients with ASD and 573 controls aged between 6.5 and 64 years old. Volumetric estimations and 3D cortical reconstructions were obtained using FreeSurfer (http://surfer.nmr.mgh.harvard.edu). As the ABIDE dataset is distributed without any quality control, intensive inspection was achieved for each subject and manual edits were used as needed. Quality control was conducted in 852 MRIs from 13 sites to date, among which 128 MRIs (15%) were excluded because of motion, artifact or poor cortical reconstruction. The resulting 724 scans were used to compare cerebral and regional cortical and white matter volumes between controls and ASD. Further analyses were conducted within the ASD group to correlate cerebral morphometry with symptoms' severity as measured with the ADOS (Autism Diagnostic Observation Scale, Lord et al.) and with IQ.

Results:

In the entire sample, no difference in global brain volume was observed in ASD as compared to controls. Trends for increased cortical volume in ASD was observed in the bilateral superior temporal gyri, right precuneus and left isthmus of the cingulate ($p<0.05$, uncorrected for multiple comparisons). Within the ASD group, patients that had higher severity of symptoms had larger cerebral volumes (cortical, white and subcortical) than patients with lower severity of symptoms (all $p<0.002$). At the regional level, this increased volume in the most severely affected patients was mostly lateralized in the left hemisphere, affecting prefrontal medial and lateral regions, inferior and medial temporal areas, as well as the parieto-temporo-occipital junction. We also observed that the patients with ASD with the lower IQ had smaller cerebral and white matter volume as compared with those with higher IQ.

Conclusions:

In this large sample of patients with ASD, we observed that ASD diagnosis alone was not a significant parameter related to different brain morphometry, suggesting that the clinical heterogeneity is also related to heterogeneous cerebral phenotype. Disentangling the different direction of the effect of higher symptom severity and lower cognitive abilities may help reconciliate previously divergent results and provide a framework to better understand the spectrum of neurodevelopmental pathways that can lead to autism.

**139.066 66** The Rich-Club Organization of the Brain in Autism Spectrum Disorder. M. Coffman*[1], V. Peddireddy[1], G. Cheran[1], C. Tallman[1] and J. A. Richey[2], (1)*Virginia Polytechnic Institute and State University*, (2)*Virginia Tech*

Background:

Understanding of the organization of structural and functional neural networks on a large scale has been advanced in recent years through a set of general techniques under the umbrella of graph analysis. Through applications of these and related techniques, comparisons of regional and global network parameters can be estimated and compared across groups, leading to the discovery of several previously hidden brain networks. Recently, the so-called "rich club" organization of the human brain has been documented (e.g. van den Heuvel & Sporns, 2011), revealing a surprisingly small number of subcortical and neocortical hubs that have a tendency to be more highly connected to each other than to other brain regions. This suggests that focal structural or functional abnormalities may have a greater than expected impact when localized to brain regions that are part of the 'rich-club'. Simulation of network failure in these hubs is particularly useful for investigating potential connectivity difficulties in ASD.

Objectives:

In the current study, we examined this notion in autism spectrum disorders (ASD), to test whether alterations in the morphological properties of 82 brain regions are 1) systematically different in ASD vs. Controls, and 2) whether any observed differences map onto the 12-16 regions thought to be part of the brain's rich-club.

Methods:

Resting state data from 184 subjects (79 with ASD) from the ABIDE database were analyzed. Subjects were matched on age (ASD=14.52; TD=15.81) and IQ (ASD=107.91, TD=113.15). Additionally, all subjects were collected at the same site. Regions of interest (82 regions indicated in the rich club of the brain) were

extracted for each subject and averaged by group. Minimum and maximum density measures of connectivity were computed for each group to conduct regional network analysis. Finally, network attacks were simulated for each group.

Results:

Preliminary analyses demonstrate the ability of utilizing the rich club connectome to generate adjacency matrices. These matrices are then applied to a brain connectivity toolbox capable of examining the impact of connectivity failures in ASD.

Conclusions:

Results demonstrate a potentially compromised network of connections in ASD. When network failure occurs in a rich club node, a greater detrimental impact on other connections in ASD. Thus, results indicate alterations in overall neural functioning in these individuals. Further, this analysis provides a data-driven approach to parsing well-documented heterogeneity within ASD. The relationship of real-world functioning to indices of altered connections in ASD provides a potential for targeting treatment.

**139.067 67** Volumetric and Microstructural Differences in a Mouse Model of Rett Syndrome. R. Allemang-Grand*, J. Ellegood, J. P. Lerch and R. M. Henkelman, *Hospital for Sick Children*

**Background:** Rett syndrome is a neurodevelopmental disorder caused by sporadic mutations in *Mecp2* leading to early-life disruptions in the brain and behaviour. Magnetic resonance imaging (MRI) of human Rett's patients and *Mecp2*mouse models have found large-scale volume losses within the brain, which have been attributed to the severe structural impairments of neurons and synapses found in Rett's (Saywell et al., 2006). However, a direct association between regional volume and neuronal morphology has not been studied across the entire brain.

**Objectives:** The objective of this study is to perform an analysis of the anatomical and cellular structural differences within the brain of the Mecp2$^{308}$mouse model of Rett's. Anatomical MRI was used to assess the regional volume differences between groups. Diffusion-weighted MRI was used to explore the organization and order of the cellular environment in the brain using a measure of water diffusion, called fractional anisotropy (FA). Finally, a Golgi stain will be performed to measure neuronal morphology.

**Methods:** *Mice* – Two separate cohorts of male hemizygous Mecp2$^{308}$ and C57BL/6 mice (Age = ~ 60 days) were used in the study. One cohort was used for anatomical and diffusion-weighted imaging, the second was used for the Golgi stain.

*MRI Acquisition*- A multi-channel 7.0 Tesla MRI scanner (Varian) was used to acquire images of the brain. To acquire images for an anatomical analysis, a T2-weighted, 3-D fast spin-echo sequence was used. To measure water diffusion through the micro-structural, cellular environment, a diffusion-weighted 3D Fast spin echo sequence was used.

*Data Analysis*– To visualize and compare the volumetric and water diffusion differences, the brains for each MR sequence were registered together. For the volume measurements, the individual volumes of 62 different structures were calculated. For the white matter structural changes, the FA intensity differences were measured in the same 62 structures as well as on a voxel by voxel basis. Group differences in volume or FA were calculated while controlling for multiple comparisons using the False Discovery Rate.

**Results:** Volume differences were found in many regions of the brain when comparing Mecp2$^{308}$ with wild-type mice. Of particular interest was the greater than 4% decrease in volume in the parieto-temporal cortex, corpus callosum, internal capsule, striatum and thalamus. Interestingly, although not consistent in every region, there seems to be a negative relationship between volume and fractional anisotropy, where a decrease in volume is associated with an increase in FA. We are currently in the process of quantifying neuronal morphology with the Golgi stain in these regions to determine the relationship between volume, FA and neuronal morphology.

**Conclusions:** This study provides whole-brain coverage of the volumetric and FA differences in the Mecp2$^{308}$ brain. Furthermore, we expect brain regions with increases in FA to house neurons with reduced complexity due to the lack of dendritic branches that will restrict water

diffusion. These findings will demonstrate that these whole brain imaging modalities can be use as biomarkers for monitoring treatment success in future studies that aim to reverse the structural impairments of neurons in Rett's.

## 140 Communication and Language

**140.069 69** Duration Perception of Autistic Children in the Context of Mandarin Chinese. Y. Fan[1], Y. Fan*[2], L. Yu[1], D. Huang[2], Z. Deng[1], D. Wang[2] and S. Wang[1], (1)*South China Normal University*, (2)*Guangzhou Cana School (Guangzhou Rehabilitation and Research Center for Children with ASD)*

Background: Studies of western languages (e.g. English), using speech and non-speech materials of various complexity, have consistently reported superiority of pitch perception and impaired duration perception in autistic individuals (e.g. Lepistö et al., 2005). However, pitch and duration have language-specific properties. Besides the perceptual function shared in both kinds of languages, pitch in Mandarin Chinese also has semantic function. Meanwhile duration in Mandarin Chinese does not carry higher-level semantic information as it does in Western languages. Only one research in Mandarin Chinese investigated the pitch perception of autistic children, demonstrating different results (Yu, in preparation). They observed perception deficits of lexical tone and non-lexical counterparts in Chinese autistic children, and the pitch perception superiority found in previous Western studies only remains in the pure tone condition. So far the duration perception in Chinese autistic children is still unclear. And how does language differences contribute to the incoherence of the cross-culture studies also needs a deeper discussion.

Objectives: We aimed to examine autistic children's duration perception in the context of Mandarin Chinese and tried to explain the language specific results.

Methods: The current study investigated the duration perception of autistic children in the context of Mandarin Chinese. Seventeen Mandarin speaking children with autism (14 males) and seventeen TD controls (14 males) participated in the current study. We applied the passive oddball paradigm which elicits the ERP component of Mismatch Negativity (MMN) to investigate the participants' auditory sensitivity to duration changes.Three kinds of linguistic and non-linguistic sound materials were chosen—pure tone, Chinese single character and its non-lexical counterparts.

Results: The results supported the view of language specific auditory perception. Only in the pure tone condition, did the Chinese autistic children show duration perception deficits. In the conditions of lexical materials and non-lexical counterparts, the perception inferiority disappeared and it even tends to be superiority in some electrodes in the lexical condition. This suggests that autistic children are intact in discriminating linguistic duration information in Mandarin Chinese.

Conclusions: Most of the previous studies reporting auditory abnormality of autistic individuals are based on the western languages. According to the results discrepancy between specific languages indicated by the current study, we argue that language experience would affect the auditory representations in autistic individuals. It may be the lack of social input that leads to the interruption of forming language-specific phonetic representations during their early childhood. This study would draw more attention to the issue of language specificity. Cross-culture factors needs to be considered cautiously when make conclusions in linguistic area.

**140.070 70** Expressive Language Profiles in Chinese Preschool Children with Autism Spectrum Disorders: Assessment with the Putonghua Communicative Development Inventory (Toddler Form). Y. Su*[1], L. Naigles[2] and L. Y. Su[1], (1)*The Second Xiangya Hospital, Central South University*, (2)*University of Connecticut*

Background: Recent research has highlighted the heterogeneity of language abilities in English-exposed children with autism spectrum disorders (ASD) (Kjelgaard & Tager-Flusberg, 2001), including their different trajectories in early language production (Tek et al., 2013). Little is known about expressive language profiles in children with ASD learning other languages.

Objectives: To depict expressive language profiles in Chinese preschool children with ASD via the Putonghua Communicative Development Inventory: Words and Sentences (PCDI-Toddler Form).

Methods: Parents of 26 2-5-year-old children with ASD (24 boys and 2 girls, mean = 49. 92 ± 12. 46 months) completed the PCDI-Toddler Form.

Children were divided into three subgroups - Low Verbal (LV) (n = 9, mean = 42.33 ± 10.43 months), Middle Verbal (MV) (n = 10, mean = 51.50 ± 13.96 months) and High Verbal (HV) (n = 7; mean = 57.43 ± 7.27 months), based on word production in the vocabulary checklist (LV: 0 – 69 words; MV: 70 – 392 words; HV: 393 words and above). Language abilities were compared among the subgroups and with the published TD norms (Tardif et al., 2008).

Results: (1) Word production differed significantly across subgroups (LV: 8. 44 ± 12.02; MV: 281.00 ± 70.20; HV: 564.43 ± 149.37, ps ≤ 0.002). The LV group scored less than the HV group in all the 10 items (ps ≤ 0.014) and than the MV group on 4 items (ps ≤ 0.009) in sections of "how children use words", "words and sentences" and "combining"; the MV group performed worse than the HV group on 6 items (ps ≤ 0.034). MLUs for the LV, MV, and HV groups were 0, 2.33 ± 1.07 and 3.57 ±1.69 respectively, significantly lower in the LV group than in the other two groups (ps ≤ 0.014). Sentence complexity scores differed significantly across subgroups (LV: 0, MV: 18.78 ± 12.80, HV: 49.14 ± 24.09, ps ≤ 0.045). (2) The LV group performed poorer than TD children aged 16 months in all the measures. The MV and the HV groups were matched to TD children aged 20.20 ± 0.92 and 25. 00 ± 3.27 months based on word production. The proportions of children's use of words referring to "past, future and absent objects/people" were significantly lower than the TD norms by the MV group in all the 5 items (ps≤0.002) and by the HV group in 4 items (ps≤0.001). Both groups were compatible to matched TD groups in the use of classifiers (ps ≥ 0.395), but not with possessives and tense markers (MV: ps ≤0.026; HV: ps = 0.070) or word combination (ps ≤ 0.001). MLUs were similar in the MV group but lower in the HV group. The MV group scored higher and the HV group equivalently as TD children in sentence complexity.

Conclusions: There is an overall expressive language delay for Chinese children with ASD: the LV group demonstrated a global impairment; the HV group performed generally better than the MV group, both showing difficulties in some uses of sentences and grammar than the vocabulary-matched TD groups.

**140.071 71** Adaptive Behavior Deficits in Children with Autism As Predictors of Parenting Stress. S. A. Fox*[1], K. V. Christodulu[2] and M. L. Rinaldi[3], (1)*University at Albany, State University of New York*, (2)*Center for Autsim and Related Disabilities*, (3)*University at Albany, SUNY*

Background: Previous research has suggested that parents of children with autism spectrum disorders (ASD) experience higher levels of stress than parents of typically developing children or children with other disabilities (Lecavalier, Leone, & Wiltz, 2006). Numerous factors have been proposed as potential causes of elevated parenting stress levels in this population, including lack of social support, stigma associated with the disorder, and notably, characteristics of the child with ASD (Pisula, 2011). Children with autism often exhibit challenging behaviors and marked deficits in the social, communication, and adaptive behavior domains. Literature on the exact contribution of child deficits to parenting stress is mixed; it has been argued that severe challenging behaviors are the largest contributors to parenting stress, but other studies have suggested that impaired daily living skills have the greatest impact (Estes, 2009). Currently, there is a dearth of literature examining the relative ability of specific domains of adaptive behavior deficits in children with autism to predict parenting stress.

Objectives: This study aims to discover the domain of adaptive behavior that is most predictive of high stress levels in parents of children with ASD. These findings will be used to draw conclusions about which child behaviors are the most worthwhile targets for intervention.

Methods: The preliminary sample is comprised of 23 families who participated in the Center for Autism and Related Disabilities' Parent Education Program for Families of Children Newly Diagnosed with Autism. As part of their participation in the program, each family completed the Parenting Stress Index (PSI) and the Vineland Adaptive Behavior Scales, Second Edition (Vineland-II). Multiple linear regression analysis was used to develop a model for predicting parenting stress from the adaptive behavior domains of communication, socialization, and daily living skills, as well as the child's maladaptive behavior index. The relative predictive ability of each behavior domain was assessed with an

examination of the predictors' contributions to the full model.

Results: An examination of the bivariate correlation matrix indicated extremely high correlations between the socialization domain and both the communication and daily living skills domains (.766 and .936, respectively). In order to preemptively correct for multicollinearity, socialization was removed from the model. The remaining three-predictor model accounted for 37% of the variance in parenting stress ($p$=.028). The communication domain obtained the largest beta-weight, demonstrating that it made the greatest contribution to the regression equation (β=1.61, $p$=.007).

Conclusions: This is the first study examining the relative predictive ability of adaptive behavior domains for parenting stress in families of children with autism. Data collection is ongoing, but preliminary findings suggest that communication deficits are the strongest predictor of parenting stress. When children are unable to effectively communicate their needs and wants to their parents, it is understandably a source of considerable stress for the family. Based on this link, interventions aimed at reducing parenting stress in this population should focus on increasing the child's communication skills.

**140.072 72** Assessing Language in School-Aged Children with ASD in a Virtual, Public Speaking Task. S. Torabian*[1], N. Alpers[2], L. Naigles[2], N. S. McIntyre[3], T. Oswald[3], L. E. Swain-Lerro[3], S. Novotny[3], T. Kapelkina[3] and P. C. Mundy[3], (1)*University of California Davis*, (2)*University of Connecticut*, (3)*UC Davis*

- Background: Higher-functioning children with autism (HFA) may display language on par with typical controls (TD) on standardized measures, yet not use language fluently in social contexts. The development of cost-effective paradigms to assess their language problems in realistic social contexts, though, is challenging.
- Objectives: This study examined the validity of a virtual reality public speaking language assessment for use with school-aged children with HFA. Language use was assessed across conditions that varied in social and non-social context, as well as higher versus lower attention demand task conditions.
- Methods: 150 children, age 8-16 are currently participating in a longitudinal study of attention and social, as well as academic development in children with HFA. Here preliminary data are presented on 13 HFA and 7 typically developing Age (11.6 years vs. 11.5 years) and IQ (104 vs. 108) matched controls. Children's speech was audiotaped, transcribed, and then analyzed for four measures of dysfluency ('um', 'uh', false starts, repetitions) and six measures of language use (noun types and tokens, verb types and tokens, discourse marker ('well' 'like') types and tokens. Language was assessed in a virtual reality public speaking task, in which the children viewed a virtual classroom through a head-mounted display. They were asked to answer different questions about their interests and daily activities for while addressing 9 targets around a large table in the VR classroom. There were three 3-minute conditions: In the Non-Social Attention condition children talked to 9 "lollipop" shaped forms positioned to their left and right at the table; in the Social Attention Condition children talked to 9 avatar "peers" to the left and right, and in the High-Demand Social Attention Condition they talked to 9 avatars that faded if children did not fixate them every 15 seconds.
- Results: Across the three conditions the HFA group tended to decrease in noun, verb, and discourse marker tokens use (from 89.2 to 68.8) whereas the TD group's usage increased (84.5 to 91.0). ANOVA revealed a Condition by Diagnostic Group interaction that approached significance F (2, 9) = 3.357, p = .058. In addition, the HFA group produced more false starts (7.9, SD = 5.55) and repetitions (6.4, SD = 5.27) respectively than the TD group (3.75, SD = 4.35; 2.75, SD = 3.06) and both groups tended to increase in dysfluencies across the conditions. The HFA group produced more noun tokens (M = 33.8, SD = 6.36) than the TD controls (M = 31.2, SD = 8.13).

However, the TD controls produced more verb tokens (M = 29.67, SD = 9.77) and discourse markers (M = 26.05, SD = 14.97) than the HFA group (25.8, SD = 4.8; 20.0, SD = 15.28 respectively).

- Conclusions: Preliminary data suggested that the VR paradigm revealed that children with HFA produce more dysfluencies and fewer verbs and discourse markers than controls and that their atypical language use may be affected by social and high attention demand contexts. Additional data will be presented.

**140.073 73** Categorical Speech Perception Across the Autism Spectrum and Its Relation to Cognitive and Language Ability. M. E. Stewart*[1], A. M. Petrou[1] and M. Ota[2], (1)*Heriot-Watt University*, (2)*University of Edinburgh*

Background:

Individuals with autism spectrum conditions (ASC) show superior discrimination of certain types of perceptual information (e.g., Bonnel et al., 2003) and also a tendency to process perceptual stimuli without reference to the contextual information of the percept (Jolliffe & Baron-Cohen, 1999). Consistent with these observations, adults with ASC are known to perceive exemplars along a visual spectrum less categorically (i.e., more continuously) than controls (Soulières et al., 2007). However, this pattern has not been examined in speech perception, a domain that typically exhibits categorical perception (e.g., Abramson & Lisker, 1970).

Objectives:

To test whether adults with ASC demonstrate reduced categorical perception of basic speech sounds and whether this effect is independent of IQ and/or language functioning that are known to affect speech perception.

Methods:

Twenty adults with High-Functioning Autism or Asperger's syndrome (HFA/AS; *mean age*=27.3, *SD*=7.8; *males*=13) were compared with 20 nonverbal IQ-matched typically-developed adults (*mean age*=27.7, *SD*=9.7; *males*=7).
Participants were given measures of autistic traits (the Autism-Spectrum Quotient; Baron-Cohen et al., 2001a), nonverbal IQ (Raven's Advanced Progressive Matrices; Raven, Raven, & Court, 1998), verbal IQ (Mill Hill Vocabulary Scales; Raven, Court, & Raven, 1988), 5 language measures, the Autism Diagnostic Observation Schedule (Lord et al., 1999), and an ABX speech discrimination task. The A and B stimuli in the ABX task were two samples taken from a /gi/-/ki/ continuum that differed in voice-onset time by 20 ms. Categorical perception of these stimuli should be manifested in higher accuracy scores around the midway point of the continuum where the boundary between the /gi/ and /ki/ categories lie.

Results:

There was a significant main effect of Step ($F$(4, 152)=8.38, $p$<.001, $\eta^2_p$=.18); accuracy was significantly better at Step 30-50 ms than at Steps 10-30 ms ($p$<.05), Step 40-60 ms ($p$<.01), and 50-70 ms ($p$<.001). There was no significant main effect of Group ($F$(1, 38)=.13, $p$=.72, $\eta^2_p$=.00) or Step x Group interaction ($F$(4, 152)=2.13, $p$=.08, $\eta^2_p$=.05). In order to test for the influence of IQ the sample was split at the median on non-verbal IQ scores. Participants with HFA/AS with below-median nonverbal IQ were significantly less accurate across the continuum ($F$(12, 136)=2.50, $p$<.01, $\eta^2_p$=.18) and they did not show the peak of performance at the boundary between phonemes ($p$<.05) compared to participants with HFA/AS with above-median nonverbal IQ. That is, there was a diminished influence of category on the discrimination of exemplars ($F$(3, 39)=3.78, $p$<.05). This was in contrast to the median-split nonverbal IQ groups without ASC.

Conclusions:

A diminished influence of category on the perception of exemplars occurs for speech signals across the autism spectrum as seen in the visual domain (Soulières et al., 2007). There is a significant ASC x IQ interaction for performance on this task. Further research is needed to assess whether reduced categorical perception can occur for other voicing continua in individuals with ASC. Implications in terms of speech processing and training on speech tasks in individuals with ASC need to be explored.

**140.074 74** Children's Differing Patterns of Discourse Marker Use in ASD and Typical Development. M. Rouhizadeh*[1], J. van Santen[1], R. Sproat[2], K. Gorman[1], P. Heeman[1], A. P. Hill[1], S. Bedrick[1], E. T. Prud'hommeaux[3] and G. Kiss[1], (1)*Oregon*

*Health & Science University*, (2)*Google, Inc.*, (3)*University of Rochester*

**Background**:

Appropriate use of discourse markers (DMs) such as 'and', 'ok', or 'wait', is important for conversational reciprocity. Based on deficits in social communication and interaction being core symptoms of autism spectrum disorder (ASD), we hypothesize atypical use of conversational DMs in ASD. Plausibly because of the effort of annotating conversations, few studies have tested this hypothesis. However, new computational text analysis tools exist that may be adapted for quantitative characterization of DM use in ASD.

**Objectives**:

(1) To develop text analysis tools for detecting DMs and for determining whether the examiner asked a question and, if so, whether it is a yes/no (YN) or a WH (e.g., 'who', 'where') question. (2) To apply these tools to transcripts of ADOS conversations involving children with ASD or typical development (TD).

**Methods**:

*Participants.* Participants were children ages 4-8, 44 with TD and 50 with ASD, age-matched. ASD diagnosis utilized the ADOS revised algorithm, the Social Communication Questionnaire, and DSM-IV-TR-based clinical consensus. Also a subset of the ASD group was selected (ASD without language impairment, or ALN group; N=24) with a CELF Core Language Score above 85, VIQ- and NVIQ-matched to the TD group.

*DMs.* Algorithms were developed to extract DMs from transcripts, distinguishing between acknowledgments (ACK: 'yes', 'no', 'hmm', 'ok', 'right', 'uhhuh') vs. non-acknowledgement DMs (nACK: 'then', 'but', 'well', 'oh', 'so', 'wait', 'actually').

*Context*. Algorithms were developed to determine whether the examiner asked a question (Q), a YN question, a WH question, or not a question (nQ).

*Measure*. For each context (Q, YN, WH, or nQ), we calculated the percentage of child turns containing nACK or ACK markers.

**Results:**

Results were the same for the TD vs. ASD and TD vs. ALN comparisons and are not discussed separately. The ALN group and the remaining ASD group did not differ on any measures. We specify the following planned contrasts: (Q vs. nQ, WH vs. nQ, YN vs. nQ.

*ACK markers*. Across contrasts, the TD group used significantly more ACK markers than the ASD group in the Q, WH, and YN contexts ($p<0.01$), with a non-significant trend in the nQ context. A non-significant Group x Context interaction indicated a trend for the TD group to change DM more with context than the ASD group.

*nACK markers.* Across contrasts, only in the nQ context did the TD group show more nACK marker use than the ASD group ($p<0.005$); moreover, the Group x Context interaction was significant ($p<0.001$), again with context having a larger effect for the TD group than for the ASD group.

**Conclusions**:

The ASD group used fewer DMs overall than the TD group. In addition, the TD group adjusted its use of nACK markers to context more than the ASD group, showing greater responsivity to the examiner's intentions. The results show also that the group differences are not due to language impairment. We conclude that these results lend support to our hypothesis and that, moreover, patterns of DM usage may provide a convenient and robust ASD-specific behavioral marker.

**140.075 75** Detection of Syllable Stress in Autism Spectrum Conditions. N. Kargas*, B. Lopez, V. Reddy and P. Morris, *University of Portsmouth*

Background: Prosody plays an important role in a range of communicative functions that have been categorized as affective, pragmatic and grammatical (Roach, 2000). Previous studies on prosody perception in autism spectrum conditions (ASC) using complex speech paradigms have reported strong evidence for impairments in the processing of affective and pragmatic/interactional cues (see review O'Connor, 2012). A possible explanation for these difficulties may stem from lower level ability in acoustic perception of linguistic information in ASC. In particular, the perception of word stress has been shown to play a crucial role for language acquisition and phonological awareness (e.g., Kaye, 1988).

Objectives: This study aimed to explore the possibility that the prosodic deficits observed in ASC may be stem from difficulties in the detection of prominent patterns of syllables within a word by using a simple speech paradigm to assess acoustic detection of syllable stress in adults with and without ASC.

Methods: A same-different stress perception task (Leong et al., 2010) was administered to a sample of 21 adults with high-functioning ASC and 21 IQ and age matched controls to assess discrimination ability of syllable stress differences between pairs of identical 4-syllable words (i.e. DEmocracy – deMOcracy). Also, the Communication Checklist-Self Report (Bishop, Whitehouse & Sharp, 2009) was used to assess three domains of communicative skills (language structure, pragmatics, social engagement). The protocol for the study received ethical approval from the University of Portsmouth Ethics Committee which follows the guidelines of the British Psychological Society.

Results: The results showed that the ASC group found it significantly more difficult than the comparison sample to judge stress between pairs of identical words. Also, correlational analyses demonstrated an association between syllable stress perception and pragmatic skills in ASC.

Conclusions: To our knowledge this is the first evidence for syllable stress perception deficits in ASC and for a link between syllable stress perception and pragmatic skills. Our findings that high-functioning adults with ASC show impairments in speech processing, suggest the possibility of more severe deficits in low-functioning ASC. Intact detection of intonational and rhythm patterns of speech is crucial for linguistic, cognitive, emotional and social development (e.g. Murray, 1992; Matychuk, 2005). A better understanding of the difficulties people with ASC have with interpreting syllable stress could potentially help us understand why these individuals display impairments in the processing of linguistic, affective and pragmatic information.

**140.076 76** Development of Pragmatic Language Understanding in Children with Autism Spectrum Disorder. K. Asada*[1], S. Itakura[2], M. Okanda[3], Y. Moriguchi[4], K. Yokawa[5], K. Konishi[5], S. Kumagaya[1] and Y. Konishi[6], (1)*The University of Tokyo*, (2)*Kyoto University*, (3)*Kobe University*, (4)*Joetsu University of Education*, (5)*Sukusuku Clinic for Child Konishi*, (6)*Doshisha University*

Background: Pragmatic language ability is defined as the ability to use and understand language in a social context for the purpose of communication. Researchers have found pragmatic language deficits in children and adults with autism spectrum disorder (ASD) (Surian et al., 1996; Paul et al., 2009). However, few studies focused on the development of pragmatic language understanding in children with ASD.

Objectives: We examined how the performance of children with ASD and typically developing (TD) children changed across ages and explored which conversational rules (i.e., Gricean maxims) children with ASD had difficulty understanding by using the Japanese version of Conversation Violation Test (CVT-J).

Methods: Participants were 13 children with ASD (mean age: 6 years 10 months; range: 5 years 2 months to 9 years 7 months) and 13 TD children (mean age: 6 years 9 months; range: 5 years 1 month to 9 years 5 months), individually matched on chronological age and sex and group-matched on IQ. The CVT-J consisted of the following five types of questions based on Gricean maxims: Relation (be relevant to the topic), Quality (be truthful and avoid saying something lacking adequate evidence), Quantity I and II (avoid less (I) or more (II) information than is required for the current purposes of the conversation), and Politeness (be polite). Each maxim had five questions, and the total number of questions was 25. Children watched a scenario that featured three hand-puppets engage in question-exchange communication: one puppet was a questioner and the other two were responders. One responder gave a correct answer and the other gave an answer that violated one of the Gricean maxims. The experimenter asked children to select the puppet that gave the wrong answers.

Results: Overall, TD children performed better on the CVT-J than children with ASD (mean score: ASD 17.5; TD 21.4, $p < .05$). In order to determine which conversational rules children with ASD have difficulty understanding, we compared the performance of the ASD group with that of the TD group in each conversational rule. We found that TD children performed better than children with ASD in the maxims Quality and Quantity I (ps $< .05$). Change of the performance

across ages (difference in slope) did not significantly differ between the groups. At a certain age (ASD: around 8 years, TD: around 6 years), both groups passed 80% correct.

Conclusions: Two important findings were obtained. First, TD children performed better than children with ASD on certain conversational rules. Second, children with ASD understood this task well (80% correct) by around eight years old, although the performance of the ASD group followed that of the TD group across ages. We discuss whether children with ASD have specific difficulty understanding some conversational rules and the ways that children with ASD can more easily understand conversational rules.

**140.077 77** Do Mandarin-Speaking High-Functioning Children and Adolescents with Autism Spectrum Disorders Use Intonation in the Resolution of Ambiguous Sentences?. Y. Su* and L. Y. Su, *The Second Xiangya Hospital, Central South University*

Background:

English-speaking high-functioning adolescents with autism spectrum disorders (ASD) demonstrated difficulties in using prosody to resolve syntactic ambiguities (Diehl et al., 2008), despite their relative strengths in processing grammatical prosody in simple sentences (e.g., Chevallier et al., 2009; Paul et al., 2005). Little is known about how children and adolescents with ASD develop and perceive grammatical prosody in other languages.

Objectives:

This study explores whether high-functioning Mandarin-speaking children and adolescents with ASD use intonation (i.e., level intonation vs. rising intonation) in disambiguating the statement reading vs. the question reading of sentences with the *wh*-word *shenme* 'what'.

Methods:

Twenty-eight 4-15-year-old high-functioning children and adolescents with ASD and 28 matched TD controls (further divided into young/old subgroups, means = 6; 7 and 11; 8) participated in a computer-based Question-Statement task (cf. Zhou & Crain, 2011), in which they either judge the truth/falsity of statements or provide answers to questions. Two Prosody Conditions (Prosody-S and Prosody-Q) assessed the participants' sensitivity to intonation in resolving ambiguous sentences with *shenme*, e.g., *Xiaohouzi meiyou chi shenme shuiguo*: the level intonation on *shenme* makes a statement, e.g., *The monkeys didn't eat any fruit*; whereas the rising intonation on *shenme* denotes a question, e.g., *What kind of fruit did the monkeys not eat?* Two Structure Conditions (Structure-S and Structure-Q) examined their knowledge of the statement reading vs. the question reading of *shenme*in unambiguous sentences, in which the syntactic/semantic structures alone determined the interpretations.

Results:

ANOVA tests revealed a main effect of condition ($F(3, 78) = 2.816$, $p = 0.045$) and a marginal effect of diagnosis ($F(1, 26) = 3.205$, $p = 0.085$) for the ASD/young and the TD/young groups. The ASD/young group performed poorer than the TD/young group in the Prosody-S condition (71.43% vs. 87.50%) and the Structure-S condition (69.64% vs. 94.64%), with the latter reaching significant difference ($t(26) = -1.974$, $p = 0.059$). But both groups performed equally well in the Prosody-Q (83.93% vs. 85.71%) and the Structure-Q (100% for both) conditions. Moreover, the ASD group's performance demonstrated a developmental trend, showing a main effect of age ($F(1, 26) = 8.054$, $p = 0.009$) and a condition x age interaction ($F(3, 78) = 2.693$, $p = 0.052$). The ASD/old group performed significantly better than the ASD/young group in the Prosody-S condition ($t(26) = -2.511$, $p = 0.019$) and the Structure-S condition ($t(26) = -2.645$, $p = 0.014$), and they performed compatibly well as the TD/old group, with correct response rates at ceiling (91.07% to 100%) across conditions.

Conclusions:

Mandarin-speaking children with ASD are less efficient than controls in assigning the statement reading (but not the question reading) of *shenme* in ambiguous sentences. This may not merely be attributed to their less sensitivity to the level intonation, rather they show delayed knowledge of the statement reading of *shenme* even in unambiguous sentences. Mandarin-speaking adolescents with ASD, with improved knowledge of the statement reading of *shenme*, demonstrate unimpaired use of intonation in resolving ambiguous sentences with *shenme*.

**140.078 78** Engaging Children with Autism Spectrum Disorder in Shared Book Reading: For Whom Does Dialogic Reading Work?. V. P. Fleury*[1] and I. S. Schwartz[2], (1)*University of North Carolina at Chapel Hill*, (2)*University of Washington*

Background: Reading aloud to children is a common practice during early childhood. While no one style of book reading may be best for all children, actively participating during reading activities (e.g., initiating comments, posing questions, responding to questions) is almost always better than passive listening that can occur when adults simply read the text. Dialogic reading is a particular method of shared story reading in which the adult uses specific question prompts to encourage children to talk during reading. There is, however, limited research that examines the appropriateness of dialogic reading strategies for children with Autism Spectrum Disorders (ASD). Specifically, little is known about the quality of engagement in shared reading activities for this population who may particularly have difficulty engaging in shared reading due to social-communication difficulties that are characteristic of the disorder.

Objectives: To determine the effect of modified dialogic reading on the following outcomes for children with ASD: (a) participation during book reading performance, and (b) knowledge of vocabulary specifically targeted in books. Because individuals with Autism Spectrum Disorders (ASD) show great variability in the expression and severity of their behavioral symptoms, we also examined whether measures of ASD severity related to differences in these outcomes.

Methods: We used a multiple baseline design across participants to examine the effect of a modified dialogic reading approach on active participation in 9 preschool children with ASD who, at minimum, had flexible phrase speech. Baseline book reading sessions consisted of school personnel reading to children "as they would normally." Intervention book reading sessions consisted of school personnel reading to children using a modified dialogic reading approach. Teacher/child dyads selected one book to read for the entire week. Children's level of active engagement -- defined as the rate of verbal participation per minute -- was coded from video. A member of the research team administered a book-specific vocabulary test at the beginning of the week and again at the end of the week in order to assess gains in vocabulary knowledge.

Results: Children were matched for ASD severity based on Autism Index scores on the Gilliam Autism Rating Scale. Visual analysis reveals that all children, regardless of ASD severity, demonstrated a similar pattern of active engagement during book reading. Baseline book reading resulted in consistently low levels of verbal participation followed by an immediate increase in verbal participation during dialogic book reading sessions. Similarly, ASD severity does not appear differentially affect vocabulary growth. Compared to baseline book reading, dialogic book reading resulted in greater gains in book-specific vocabulary for all children.

Conclusions: Modified dialogic reading was effective in improving active participation for all children who participated in the present study, regardless of ASD severity. Actively participating in book reading also appears to have collateral benefits in vocabulary knowledge. In light of the preliminary outcomes in this study, we suggest that dialogic reading techniques may be a promising practice that can be incorporated in early intervention programming for children with ASD pending further rigorous study that replicate and extend these findings.

**140.080 80** Examining Language Outcomes from a Naturalistic Language Intervention for Minimally Verbal Children with Autism. L. H. Hampton*, S. Thrower and A. P. Kaiser, *Vanderbilt University*

Background:

The use of an Augmentative and Alternative Communication (AAC) device with minimally verbal children has shown to be successful in increasing spontaneous language during an naturalistic language intervention (Olive et al., 2006). It is crucial to the development of phrase speech and increased social communication to find an effective method for systematically teaching verbs so that children can develop phrase speech. Both Enhanced Milieu Teaching (EMT) and Joint-Attention, Structured-Play, Emotion Regulation (JASPER) paired with the use of an AAC device have been shown effective interventions for increasing spontaneous language (Kasari et al., submitted) . The current study examined the effects of these interventions with and without the

use of an AAC device in relation to the amount of verbs gained with minimally verbal children.

Objectives:

The following questions were addressed in this study: (a) Do parents of children who receive intervention with the AAC report more language use and or verb use than parents of children participating in the spoken language intervention? (b) Is child verb use higher in a naturalistic language sample for children who received the intervention with the AAC versus children who received the spoken language intervention only?

Methods:

The participants included 20 minimally verbal children with autism (Mean age=6.46 years, SD=1.11). Participants were randomly assigned to either JASP-EMT with an AAC device or JASP-EMT with spoken language only. All participants received two 45-minute sessions each week for 12 weeks of intervention. Parents completed MacArther-Bates Communication Development Inventories (MCDI) at the pretest and at the end of the 12-week intervention. 20-minute language samples were transcribed and coded from prior to and following intervention.

Results:

Parents of children who received the JASP-EMT intervention with the AAC device during intervention reported more words produced and understood (M=58.8, SD=84.4) as compared to children who received JASP-EMT with spoken language alone (M=-44.6, SD=130, d=.95). The difference between the groups is approaching significance (t=1.9 p=0.068). Parents did not report differences between groups in verb use (t=13.1, p=0.677). However, across parents in both groups verb use improved by an average of 9.5 verbs in 12 weeks (SD=16.2). Children who received the intervention with the AAC did not produce significantly more verbs in the language sample than children who received spoken language alone (t=.901, p=.38).

Conclusions:

Parents of minimally verbal children with autism reported that their children produced and understood more words after an intervention using JASP-EMT with AAC device than children who received the JASP-EMT intervention using spoken language alone. Although parents did not report differences in verb use between groups, overall improvement in verb use was reported by parents in both groups. Children did not produce more verbs in a naturalistic language sample, indicating that the AAC did not facilitate verb use. Future research is necessary to examine specific teaching of different parts of speech for minimally verbal children with autism. Implications for practice include combining an AAC with naturalistic language strategies, which may increase words produced by minimally verbal children.

**140.081 81** Gesture and Speech Production Indicate Audience Hypersensitivity in ASD. L. Morett*, A. Lynn, B. Luna, K. O'Hearn and A. Ghuman, *University of Pittsburgh*

Background:

Communication and perspective taking are problematic for individuals with autism spectrum disorder (ASD). Although these phenomena have been studied individually in ASD, little research has investigated the intersection between them. When speaking to a face-to-face interlocutor, individuals with ASD produce more pauses than their typically developing (TD) counterparts (Lake, Humphreys, & Cardy, 2011), suggesting that spoken communication is taxing for them. Gesture is particularly informative because it communicates conjointly with speech (Kendon, 1980; McNeill, 2005) and reflects speakers' sensitivity to listeners' needs (Alibali, Heath, & Myers, 2001). However, few studies have investigated how individuals with ASD produce it in conjunction with speech. In order to determine whether audience awareness affects verbal and non-verbal communication in ASD, it is necessary to examine how individuals with ASD gesture when communicating with visible and non-visible interlocutors.

Objectives:

In this study, we examined ASD and TD adolescents' gesture and speech production when speaking to a visible or non-visible interlocutor.

Methods:

37 adolescents were recruited and tested individually: 16 diagnosed with ASD (age: M=15.53, SD=0.79; FSIQ: M=104, SD=4.25),

and 21 TD controls (age: M=16.0, SD=0.50; FSIQ: M=108.6, SD=1.84). Participants viewed a short cartoon video clip and retold what happened in the clip to an experimenter sitting across a table who was either unobstructed or behind an opaque cardboard screen. This process was then repeated with another clip from the same video, and the experimenter in the opposite condition (visible or non-visible). Sessions were discreetly video recorded and were later transcribed and coded using ELAN software (http://www.mpi.nl/tools/). To facilitate comparison with other studies, McNeill's (2005) gesture coding scheme was used, and gesture production was normalized by speech production.

Results:

Overall, participants produced more gesture in the visible than the non-visible condition, and participants with ASD produced less speech and gesture than their TD counterparts. Between-group differences were smaller in the non-visible condition, with participants with ASD producing more speech and gestures when their interlocutor was not visible. ASD and TD participants were similar in iconic and pointing gesture production within the visible and non-visible conditions. However, TD participants produced more metaphorical and emphasis gestures than participants with ASD in both the visible and non-visible conditions. Additionally, across conditions, ASD participants proposed fewer discourse markers (um, uh, etc.) and more pauses in their speech than TD participants.

Conclusions:

This work provides evidence that differences in gesture production observed in individuals with ASD are caused by hypersensitivity to the presence of a listener, rather than general speech or motor problems. The results suggest that some of the communication abnormalities associated with ASD may arise from reduced perspective-taking ability. The findings that the gestures of adolescents with ASD were less numerous in the visible condition relative to the non-visible condition suggest that face-to-face interactions are cognitively taxing for individuals with ASD, which negatively affects their communication ability. These data suggest that speech and gesture in high functioning individuals with ASD show relatively mild abnormalities that become greatly exacerbated when they become visibly aware of their listeners.

**140.082 82** Heritability of Pragmatic Language in Autism Spectrum Disorder: A Study of Twins. V. Y. Kang*, K. Levesque, A. Anderson, A. Kresse, S. Faja, E. E. Neuhaus, R. Bernier and S. J. Webb, *University of Washington*

Background:

Environmental and genetic factors both influence the development of Autism Spectrum Disorder (ASD) (Hallett et al., 2012). Some evidence for a strong genetic component in ASD comes from twin studies, which have found rates of concordance for the disorder to be higher among monozygotic (MZ) twins relative to dizygotic (DZ) twins (Hallmayer et al., 2011). Additional support comes from the study of the broader autism phenotype (BAP) in which unaffected first degree relatives of individuals with autism display some ASD traits (Constantino et al., 2010; Toth et al., 2007).

Studies have shown that genetic factors have a strong influence on communication in individuals with autism (Hallett et al., 2012). Specifically, deficits in pragmatic language are not only one of the consistent impairments found in ASD, but also a result of a genetic component (Tager-Flusberg, 2005; Baron-Cohn, 1988; Bishop et al., 2006). Impairment in pragmatic language includes overtalkativeness, talking in a stereotypical manner, or being unable to consider others' viewpoints (Bishop et al., 2006). As pragmatic language demonstrates an understanding of social cues and norms, it could be used as a method of measuring one's communication skills (Lam et al., 2012).

Objectives:

This study will investigate pragmatic language impairments in a twin ASD population. If pragmatic language has a genetic component, there should be a higher degree of similarity in pragmatic language ability within MZ twin pairs compared to DZ twin pairs.

Methods:

19 MZ twin pairs (14 TD, 5 ASD) and 17 DZ pairs (5 TD, 12 ASD) between the ages of 5 and 22 participated in the study (M = 10.6, SD = 4.02).

Individuals were video-recorded while they completed a 15-20 minute interview from the ADOS. The videos were rated by coders blind to diagnosis. Coders assessed subjects' pragmatic language using the Pragmatic Rating Scale-Modified (PRS-M) (Ruser, 2007), which scores subjects on both verbal (e.g., clarity, referencing emotions, grammar) and non-verbal (e.g., eye contact, gestures) aspects of pragmatic language.

Results:

Typically developing (TD) individuals showed significantly better pragmatic language (evidence by lower PRS-M sum of scores) (M = 9.21, SD = 3.48) compared to the ASD group (M = 13.52, SD = 3.07) (F (1) = 16.19, p = .00) confirming that pragmatic language is an impairment in the ASD sample.

The intra-class correlation for MZ and DZ pairs were analyzed with SPSS. PRS-M sum scores of MZ twin pairs showed a strong correlation (ICC (19) = .85, p = .00). PRS-M sum scores were not related within twin pairs for DZ twins (ICC (17) = .45, p = .13).

Conclusions:

Pragmatic language ability showed strong concordance within MZ twins but not DZ twins, suggesting that it may have a genetic basis. Given its potential genetic basis and its sensitivity to ASD impairment, it may have potential to be an endophenotype of ASD.

**140.083 83** Imitation Skills in Children with Autistic Spectrum Disorder in Different Stimulation Situations. A. C. F. R. Souza[1], A. C. Tamanaha[1], A. Armonia[1], M. Bevilacqua[1], L. Mazzega[1] and J. Perissinoto*[2], (1)*UNIFESP*, (2)*Federal University of São Paulo*

Background: Several studies have shown that the inability of early imitation interferes with the social and communication skills, especially for children with Autism Spectrum Disorder. In recent years we have witnessed a significant use of technological resources such as computers and iPad, as sources of aid for modeling and facilitating the learning.

Objectives: To analyze the imitation skills of children with Autistic Spectrum Disorder in different stimulation situations.

Methods: The sample was composed of 20 children, 16 boys and 4 girls aged in between 3 and 12 years, diagnosed with Autistic Spectrum Disorder according to the diagnostic criteria of the DSM-IV (APA, 2002) and ICD-10 (OMS, 1998). We have conducted the Imitation Test (Takiuchi, Befi-Lopes, 2000) composed of imitation of simple and sequential gesture schemes. Nine simple gestures and four sequential actions were added to the original proposal, so that a total of 18 gestures and 8 actions were randomly grouped into two forms of presentation: on a computer screen and personally. These simple and sequential gesture schemes represent everyday actions, eg: to imitate the gesture of drinking from a cup, or to imitate the actions of putting the doll to sleep. The implementation of tasks in both on the computer screen and personally was made by the same Speech and Language Therapist. The children were placed in front of her or the computer screen and received the instruction to observe every simple or sequential gesture schemes and play them immediately.

Results: The children had a low score of positive answers both for simple gestures and for actions, regardless of these being presented on the computer screen or personally. Therefore, there was no advantage in using different stimulation situations. There was a significant correlation between receptive vocabulary and intellectual level in some of the sequenced actions.

Conclusions: It was possible to analyze the imitation skills of children with Autistic Spectrum Disorder in different stimulation situations and to verify that, in general, the children had difficulty in imitating gestures and sequenced actions presented both on the computer screen and personally.

**140.084 84** Impact of the Temporal Dynamics of Speech and Gesture on Communication in Autism Spectrum Disorder. A. Lambrechts*, K. Yarrow and S. B. Gaigg, *City University London*

**Background:** Autism Spectrum Disorder (ASD) is characterized by difficulties in communication and social interaction. Abnormalities in the use of gestures or flow of conversation are frequently amongst the clinical observations that contribute to a diagnosis of the disorder but the mechanisms underlying these communication difficulties remain unclear. While studies in children show a reduced use of co-speech gestures overall (e.g. Sowden et al., 2013), de Marchena and Eigsti (2010) found that in adults some gestures are

used with similar frequency in ASD and TD populations, but that gestures produced by ASD individuals are less strongly time-locked to speech than in TD individuals. This may indicate that abnormal temporal processes contribute to impaired social skills in ASD (Allman, 2011).

**Objectives:**

- Characterise the temporal dynamics of speech and gesture coordination in ASD in naturalistic speech

- Quantify the use of gestures in ASD

- Test the hypothesis that atypical temporal coordination between speech and gestures results in a lesser quality in communication

**Methods:** The context of a previously published study of memory in ASD (Maras et al., 2013) provided the opportunity to examine video recordings of 16 ASD and 17 TD adults attempting to recall details of a standardised event they had participated in (a first aid scenario). The current analysis was designed to quantify the participants' communicative behaviours in three ways: 1) Segmenting the videos to identify each gesture and document its precise timing aimed to establish whether gestures are used differently in ASD and TD participants; 2) Extracting the quantity of movement as well as the pitch and volume of speech over time allowed us to characterise whether gestures were time-locked to speech similarly in ASD and TD individuals; 3) Collecting subjective ratings on the quality of communication displayed in the audio-only or audio-visual recordings helped to establish to what extent the use of gestures improved the quality of communication in ASD and TD participants.

**Results:** Overall, our results indicated no main group difference in the use and coordination of speech and gesture: both groups produced the same quantity of movement over time ($t(33)=-0.165$, $p>.8$), and gestures were produced within the same time window and with a similar distribution by ASD and TD individuals ($\eta^2_p=.042$). Similarly, no group differences were found in the subjective ratings on the quality of communication: in both groups the use of gestures improved comprehension and engagement from the listener. Interestingly, in line with previous report, we found that ASD individuals spoke on average louder than TD individuals ($t(33)=-3.520$, $p<.005$). Notably, all measures showed a large inter-individual variability in both groups.

**Conclusions:** The current data do not suggest that ASD individuals experience more difficulties than TD participants in time processes relevant to communicating personally experienced events. However large inter-individual differences could contribute to communication difficulties in some participants. It will be important for future studies to examine the timing of communicative behaviours during reciprocal interactions, that place demands not only on coordinating speech with gesture but to coordinate one's own behaviour with that of others.

**140.085 85** Investigating the Shape Bias for Word Learning in Children with Autism Spectrum Disorders. E. Potrzeba*, D. A. Fein and L. Naigles, *University of Connecticut*

**Background:**

Research in word learning strategies for children with autism spectrum disorder (ASD) has shown that children with ASD parallel typically developing (TD) children with word learning strategies such as the noun bias and mutual exclusivity[1]. However, they have not been shown to display a shape bias, which occurs when children extend a novel word to objects of the same shape, rather than to other physical features such as color or texture[2]. Previous demonstrations of children with ASD lacking a shape bias included only a small sample (n=15) and restricted age range; moreover, performance correlated with standardized test scores, suggesting that some children with ASD did exhibit a shape bias. We hypothesized that subgroups of children with ASD may have the ability to use the shape bias for word learning.

**Objectives:**

Extending Tek et al., (2008) we increased the participant total to 32 children with ASD and collected data across 6 visits rather than 4. This allows us to look for subgroups and for a later-emerging shape bias. Error analyses were conducted to investigate alternative looking patterns.

**Methods:**

Children with ASD (*n*=32, *M* Mullen EL=17.5, *SD*=7.2, *M*-RL=21.1, *SD*=9.2) were matched with TD children (*n*=35, *M* EL=20.5, *SD*=5.1, *M*-RL=20.9, *SD*=3.6) at visit 1 of a longitudinal study. Children were visited every four months. The shape bias was tested with the intermodal preferential looking (IPL) paradigm: Five novel objects were presented, each was followed by two options; one matched the original in shape while the other matched the original in color. During the first (NoName) presentation of each set, the baseline audio asked "Which one looks the same?" During the second (Name) presentation, the original object was given a label (e.g., "dax") and the test audio asked "Where is the dax?" Children who looked longer at the shape match during the Name trials than during the NoName trials demonstrated a shape bias.

**Results:**

TD children showed the shape bias at 20 months ($t(22) = -1.787$, $p<.05$, one-tailed) and at each subsequent visit ($t(30)$s > 2.0, $p$s<.05). Children with ASD did not show a significant shape bias, as a group, at any visit ($p$s>.11). Children with ASD's errors primarily involved looking longer at the color match (18.8% of all trials) during the test trials across visits; fewer children simply looked at shape (8.8%) or color (11.5%) during both NoName and Name trials. Eighty percent of TD children demonstrated a shape bias in over 60% of their visits. In contrast, the majority of children with ASD showed a shape bias on fewer than 60% of visits; however, three children did show a shape bias at all visits and ten others at more than 60% of visits.

**Conclusions:**

Even at 52 months, most children with ASD did not show a shape bias; however, we did observe several children exhibiting the bias consistently. Further analyses will scrutinize the language and socialization levels of the children who did vs. did not demonstrate a shape bias to investigate the origins of shape bias abilities and difficulties.

**140.086 86** Item-Level Analysis Demonstrates Significant Differences in Word Production and Understanding at 12 Months of Age in Children at Risk for Autism. D. C. Lazenby*[1], G. Sideridis[1], P. S. Dale[2], M. F. Prante[3], N. Coman[1], N. L. Huntington[4], C. A. Nelson[1] and H. Tager-Flusberg[5], (1)*Boston Children's Hospital*, (2)*University of New Mexico*, (3)*Utah State University*, (4)*Boston Children's Hosptial*, (5)*Boston University*

Background: Autism Spectrum Disorder (ASD) is characterized by persistent deficits in social communication and social interaction as well as restricted, repetitive patterns of behavior, interests or activities. Several studies, including prospective infant sibling studies, have identified delayed babbling, verbal expression and regression in children with ASD. Preschoolers with ASD show greater impairment in receptive compared with expressive language abilities. The recently released DSM-5 eliminated language delay as a diagnostic criterion because it is not specific to ASD. It instead emphasizes qualitative language deficits in conversation, integrated verbal communication, stereotyped or repetitive speech (echolalia, idiosyncratic phrases), and ritualized patterns of verbal behavior (greeting rituals). No published research identifies qualitative word use differences in infants who develop ASD.

Objectives: The purpose of this study was to investigate qualitative differences between ASD and typically developing children in terms of word production and understanding as measured on the McArthur-Bates Communicative Development Inventories (MBCDI).

Methods: Item Response Theory (IRT) was applied to determine the relative probability of understanding and producing each of the 396 words on the MBCDI. Differential Item Functioning (DIF) was calculated to determine which words understood or produced favored ASD or typically developing (TD) children given equivalence in their levels of ability. Participants for this cross-sectional analysis were part of a larger ongoing study of infant siblings at risk for ASD. We analyzed 15 later-born siblings with ASD, and 33 TD controls, followed from 6 months of age through 36 months or until they dropped out. Diagnosis was based on ADOS classification and independent clinical confirmation.

Results: At 12 months of age, 14 words were associated with Differential Item Functioning (DIF). These words were significantly more or less likely to be produced or understood as a function of grouping (TD versus ASD children). Two words were significant in terms of production. "Hi" was significantly more likely to be produced by TD children and "block" was significantly more likely

to be produced by children in our ASD sample. Twelve words were significantly more likely to be understood by children with ASD - "lion, mouse, car, train, outside, rock, swing, brother, close, open, show and out." No words were significantly more likely understood by TD children.

Conclusions: The results of this study indicate there are qualitative language differences measurable at 12 months of age on the MBCDI between typically developing and ASD children. Children with ASD's significantly lower likelihood to produce "Hi" may be early linguistic evidence of reduced social communication. ASD children's significantly higher likelihood of producing the word "block" as well as understanding words related to animals, toys and objects may be an early linguistic manifestation of restricted, repetitive interests or activities. These results may also be influenced by linguistic input heard from other family members, including their affected sibling. Next Steps: We will complete an item-level analysis on high-risk siblings without autism. We will seek more participants to stabilize our 12-month estimates. We will also analyze 18-month MBCDI data for word production differences.

**140.087 87** Measurement of Crossmodal Integration of Expressive Affect Communication in Autism. J. van Santen*[1], A. Kain[1], A. P. Hill[1], E. T. Prud'hommeaux[2], R. Ludovise[1], C. Conway[3], G. Keepers[1] and E. Fombonne[1], (1)*Oregon Health & Science University*, (2)*University of Rochester*, (3)*Columbia University*

Background**:**

There is evidence for atypical functional and anatomical connectivity in autism spectrum disorders (ASDs), as well as for reduced crossmodal integration in the receptive domain – plausibly a manifestation of the former. The presence of an ADOS code called "Language Production and Linked Nonverbal Communication" suggests that reduced crossmodal integration may also exist in the expressive communication domain. However, there are few formal studies on the latter, due to a dearth of measurement methods.

Objectives**:**

The objective is to create a method for measuring crossmodal integration of expressive communication (*CIEC*), specifically affect communication, and to demonstrate this method on a sample of children with ASDs, Typical Development (TD), and Specific Language Disorder (SLI).

Methods**:**

*Participants*: Twenty-five children ages 8-11 participated: TD (9), ASD (10), and SLI (4). *Protocol*: Children were trained to re-enact a brief story, pretending to be an actor/actress. Each produced between 19 and 46 videorecorded utterances. *Modality-specific stimuli*: Each utterance recording was processed by software to generate five stimulus types: three audio-only speech-related stimuli (speech; delexicalized speech, i.e., speech rendered unintelligible; text transcripts) and two video-only motor stimuli (facial expression; gesture). *Ratings*: Eleven undergraduate students rated arousal and valence of each stimulus on 5-point scales. These ratings were subsequently averaged over raters to form pooled ratings. *Sequencing*: stimuli were blocked by stimulus type and randomized by utterance and child, making it unlikely that raters knew when two stimuli related to the same utterance. *Measurement of CIEC*: For each individual child, separately for arousal and valence, correlations over utterances were computed between the pooled ratings of the five modality-specific versions of the utterances. These *cross-modal correlations*are proposed as a measure of CIEC.

Results:

*Reliability*: The median inter-rater correlation was 0.52. We one-hundred times randomly formed two rater sub-groups and computed corresponding sub-group averages for each stimulus. The correlations between these averages ranged from 0.825 to 0.875, indicating that ratings pooled over all eleven raters had adequate reliability. Subsequent analyses used these pooled ratings. *Validity:* First, correlations among the motor modalities and among the speech-related modalities were higher than those between motor and speech-related modalities. Second, using multiple regression, speech ratings were well-predicted from delexicalized speech ratings and text ratings. Both facts confirm that the ratings behaved as expected. *Presence of CIEC:* Combining data over participants, each of the twenty pairwise cross-modal correlations was positive for both valence (mean of 0.31; $p<0.0001$) and arousal ratings (mean of 0.42;

p<0.0001). Because of the way the stimuli were sequenced and their modality-specificity, these correlations strongly suggest the presence of CIEC. *CIEC differences between groups:* Cross-modal correlations were significantly larger in the TD group than in the ASD group for valence, but not for arousal.

Conclusions:

A new paradigm was proposed for measuring crossmodal integration of expressive communication. Affect of individual utterances is rated independently in five modalities, followed by per-child crossmodal correlational analysis. Results provide evidence for the reliability and validity of the rating paradigm, and suggest that, as predicted, crossmodal integration is reduced in children with ASD.

**140.088 88** Non-Verbal Children with ASD (NV-ASD): Validating a Registry and Characterizing a Population. A. R. Marvin*[1], P. A. Law[1], J. K. Law[1], E. M. Arthur[1], E. L. Mortenson[2], A. M. Abbacchi[2], T. T. Watson[3], A. A. Westreich[1], T. Gray[4], Y. Zhang[2], D. J. Marvin[1], S. N. Levin[1] and J. N. Constantino[4], (1)*Kennedy Krieger Institute*, (2)*Washington University School of Medicine*, (3)*Washington University at St. Louis*, (4)*Washington University in St. Louis*

**Background:**

This study completes a series of verification/validation studies for a US-based, online, parent-report-based ASD registry with > 46,000 consented participants. Child probands are required to have a professional diagnosis of ASD. Previous studies have verified parent report of professional ASD diagnosis via medical record review (Daniels et al., 2012) and validated the Positive Predictive Value (PPV) of ASD diagnosis among verbal children in the registry (Lee et al., 2010). The current study is comparable to Lee et al., but limited to NV-ASD children. This study provides a unique opportunity to characterize this oft overlooked ASD subpopulation. NV-ASD presents unique challenges and opportunities for ASD research. In addition to language deficits, many additional ASD-like traits are observed at lower IQ levels in other, non-ASD, developmental disorders. This makes it difficult to accurately diagnose ASD in individuals at the lower end of the IQ scale. Thus, clinical diagnosis depends even more heavily on the clinician's best estimate in conjunction with traditional ASD assessments.

**Objectives:**

- To determine the PPV of an online parent report-based registry for NV-ASD child participants.
- To characterize NV-ASD in this population.

**Methods:**

***Eligibility:*** Enrolled in the registry; current ASD diagnosis; confirmatory score >= 12 on the SCQ-Lifetime to account for variability in the quality of community-based professional diagnoses of ASD; non-verbal per Q1 in the SCQ-Lifetime: "Is she/he now able to talk using short phrases or sentences?"; >= 6 years, an age when verbal/non-verbal status is generally established; aged <18 years.

***Procedures:*** Eligible participants were invited to receive an in-person clinical assessment at labs in Maryland, Missouri, or Michigan, or at their home in the northern-New Jersey/New York region. The clinical assessment included the ADOS, ADI-R, and one or more IQ-related tests. Parents were asked complete a battery of online questionnaires: SRS, ABAS-II, RBS-R, ABC, and the registry's proprietary basic history questionnaire. The additional questionnaires were required to help characterized the population and help to differentiate ASD in the event that the SCQ-Lifetime did not suffice. Parents were also asked to request that a teacher complete an SRS for their child. Parents were asked to produce evidence that their child had, indeed, received a community diagnosis of ASD.

**Results:**

63 children were consented and 56 participants (43 male; 77%) completed the study. 100% of participants ($CI_{95\%}$ = [95%, 100%]) were deemed by the study's expert research clinicians to have an ASD. All participants met the criteria for ASD on both the ADOS and the ADI-R. All participants had cognitive disabilities beyond non-verbal status.

**Conclusions:**

ASD research requires increasingly large samples to uncover the causes of this etiologically heterogeneous neurodevelopmental syndrome. These results suggest that scientists can both use

registry data and recruit research participants from the registry with confidence.

The relationship between degree of general cognitive impairment and the expectable severity of sub-sets of autistic symptoms (i.e., social communication and restricted/repetitive behaviors) among all non-verbal individuals warrants further study, and is being examined in this unique group of NV subjects who meet diagnostic criteria for ASD.

**140.089 89** Parents' Strategies to Elicit Autobiographical Memories in Autism Spectrum, Language Impaired and Typically Developing Children. D. N. DeNigris[1] and S. Goldman*[2], (1)*The Graduate Center, CUNY*, (2)*Albert Einstein College of Medicine*

**Background:**

Parent-guided conversations about the past promote the development of autobiographical memory, defined as explicit memory of an event that occurred in a specific time and place in one's life (Nelson & Fivush 2004). The expression of self is facilitated by narrative skills which evolve from joint reminiscing experiences -an inherently social activity- supported by shared minds, often lacking in children with Autism Spectrum Disorders (ASD). Parents are adapting their communicative styles based on their view of the child's ability to participate actively. Prior research on personal narratives in children with ASD reported organizational difficulties and a focus on details (e.g., Goldman, 2008). Therefore, children with ASD may have difficulties maintaining meaningful conversations about personal events which in turn may affect parental input and verbal transactions. Here, we focused on parents' strategies to guide their child's recall and analyzed parents' differing ways to enter into the discourse about the past.

**Objectives:**

To examine (1) negotiation among dyads regarding speaker/responder roles; (2) prevalence of directives versus elaborated questions and responses among the three groups; and (3) focus on enrichment of shared events versus memory accuracy during past event conversations among three diagnostic groups.

**Methods:**

Parent-child conversations about autobiographical memories were recorded and coded for events, length, and speaking turn type in 11 high-functioning with ASD (HFA), 11 non-autistic with developmental language disorders (DLD), and 8 typically developing (TD) children matched for chronological age and non-verbal IQ. Analyses focused on (1) parent's eliciting strategy and (2) child's response choice. Speaking turns were coded as questions (direct or elaborate), responses (direct or elaborate), non-obligatory bids for participation (comments, acknowledgments or corrections), or unrelated/irrelevant utterances.

**Results:**

No significant differences between diagnostic groups were found for number of events, length of conversation, total turns taken, and number of turns taken by parent or child. Significant differences were found in speaking turn type. HFA parents used more direct questions than TD parents. Additionally, HFA and DLD parents used more corrections than TD parents. Lastly, HFA dyads used fewer comments than TD dyads, but more unrelated/irrelevant turns than both DLD and TD dyads.

**Conclusions:**

Analysis of transactional conversations about the past provides an opportunity to examine the interplay between child's communication deficits and parents' input. As such, these results shed light onto parents' strategies and their child's response type. Specifically, HFA parents not only used more direct questions to elicit recall but also focused more on memory accuracy as opposed to TD parents who provided enrichment through elaboration. Parents of HFA and DLD children naturally adjusted their conversational style to their child's communication difficulties and used these directive strategies to ensure successful verbal exchanges. Yet, these direct questions may put the emphasis on external and factual details rather than affect and a sense of self. These results should encourage parents to value meaningful personal conversation with their child, regardless of social or language difficulties, in order to strengthen their sense of self.

**140.090 90** Prosodic Abilities in High Functioning Autism. M. Filipe*[1], S. Frota[2] and S. Vicente[1], (1)*University of Porto*, (2)*University of Lisbon*

Background: Language is crucial to human communication, and it is usually studied in terms of the words and sentences used for conveying ideas, beliefs, and instructions to others; however, other aspects of language are equally important. These other features impact not only on what we say but also on how we say it. These aspects of language are usually referred to as prosody. They include stress and prominence patterns, rhythm, phrasing and intonation, and have several communicative functions. Difficulties with prosodic skills can dramatically influence daily conversations, social interactions, and even typical language development.

Objectives: We aim to analyse prosodic impairments in a group of children with high functioning autism (HFA) compared to typically developing peers (TD), and study possible interactions with other deficits in autism.

Methods: 15 children (3 girls, 12 boys) with HFA (6 - 9 years; $M$ = 7.40, $SD$ = 1.12; IQ ≥ 70) matched to a TD group on age and gender ($n$= 15). We examined prosody (using the Profiling Elements of Prosody in Speech-Communication; PEPS-C), non-verbal intelligence, attention, executive functions, language, and receptive vocabulary.

Results: An analysis of variance (ANOVA) on the tests results obtained, with Group as a factor, showed significant differences in the following PEPS-C subtests: Turn-End Reception ($F$ (1, 28) = 5.701, $p$ = 0.024; $\eta^2$ = .169) and Focus Expression ($F$ (1, 28) = 4.490; $p$ = .043; $\eta^2$ = .138). After controlling for the effect of non-verbal intelligence, significant differences between groups were also found in the tasks Short-Item Discrimination ($F$ (1, 28) = 34.542, $p$ = 0.001; $\eta^2$ = .571), Long-Item Discrimination ($F$ (1, 28) = 23.028, $p$ < .001; $\eta^2$ = .470), Long-item Imitation ($F$ (1, 28) = 10.906, $p$ = 0.003; $\eta^2$ = .295), Turn-End Reception ($F$ (1, 28) = 61.074, $p$ < .001; $\eta^2$ = .701), Affect Reception ($F$ (1, 28) = 56.589, $p$ < .001; $\eta^2$ = .685), and Focus Reception ($F$ (1, 28) = 6.850, $p$= 0.015; $\eta^2$ = .209). No effect of the variables executive function, attention, language, and receptive vocabulary was found. To determine the contribution of non-verbal intelligence to the impaired performance in prosodic tasks, this variable was entered in a regression model as a predictor of the overall PEPS-C results. This regression model explained about 82% of the variance.

Conclusions: The effect size of non-verbal intelligence, as well as the regression model results, showed that this skill had an important explanatory role for the differences observed in prosodic abilities of individuals with autism. Consequently, it could be concluded that prosodic abilities are affected by cognitive strengths or difficulties. This result has led us to consider that different approaches of autistic cognition (driven by neural differences) can be applied to linguistic traits observed in autism. Cognitive theories can guide future research, and can help to clarify the different causes of inconsistent results in studies of impaired prosody in autism.

**140.091 91** Receptive Language Abilities in Young Children with Autism Versus Typically Developing Children. S. Malik*[1], C. Stefanidou[1], K. Kantartzi[2] and J. P. McCleery[1], (1)*University of Birmingham*, (2)*Birmingham City University*

Background: Recent research suggests a possible specific receptive language deficiency in children with autism, such that these children may have lower receptive relative to expressive language skills. However, some limitations of existing studies include the absence of a typically developing comparison control group, as well as use of parent-report measures.

Objectives: The present study aimed to explore differences in relative receptive versus expressive language skills in children with autism, compared with a typical child sample. We also explored potential associations between language abilities and autism symptom severity in the children with autism.

Methods: Participants were 44 children with ASD and 54 typically developing children, aged 2 to 6 years. Both groups underwent verbal and nonverbal cognitive assessment using the Mullen Scales of Early Learning. The Autism Diagnostic Observation Schedule (ADOS) was also administered to the autism participant group. The two groups were compared on verbal abilities, including receptive and expressive language age-equivalents, and within-subject difference scores for receptive versus expressive language (RL-EL) whereby a positive value was indicative of higher receptive language than expressive and a negative value was indicative of lower receptive than expressive language. The ASD group data

were also examined for correlations between language abilities and autism symptom severity indexed by ADOS Total scores.

Results: Both receptive and expressive language skills were found to be significantly lower in the autism group compared with the typical group ($p<0.01$). However, there was no evidence for differences in the relative receptive versus expressive language development trends or trajectories of the autism group compared with the typical group ($p=0.23$; TD mean RL-EL = 0.5, SE = 0.99; ASD mean RL-EL = -0.6, SE = 1.1). Furthermore, in the autism group, language scores (receptive and expressive average) were moderately negatively correlated with ADOS Total scores ($r=-.48$, $p<0.01$).

Conclusions: These results indicate that the children with autism had clear deficits in both receptive and expressive language when compared with typically developing children. However, although the mean difference between receptive and expressive language (RL-EL) abilities was found to be numerically negative for children with autism and positive for typical controls, this difference did not nearly approach statistical significance. Thus, the current results do not support the hypothesis of a specific receptive language deficiency in young children with autism. Although some previous studies have uncovered evidence for a specific receptive language deficit in children with autism, some of these studies used developmentally delayed control children who exhibited a tendency for impaired expressive relative to receptive language abilities. Furthermore, the current findings are consistent with recent findings of Kover et al (2013), who also found no evidence for a relative receptive versus expressive language deficiency in autism compared with typical controls; but did find an impoverished rate of receptive versus expressive language development with age in this population. Therefore, specific receptive language differences in childhood autism may be a result of early learning differences such that RL-EL performance differences do not become apparent until the children are somewhat older.

**140.092 92** Selective Listening in Autism: The Influence of Informational Masking. I. F. Lin*[1], T. Yamada[2], M. Nakamura[2], H. Watanabe[2], Y. Takayama[2], A. Iwanami[2], N. Kato[2] and M. Kashino[1], (1)*NTT Communication Science Laboratories*, (2)*Showa University*

Background: In a noisy environment, the difficulty to hear out the target speech can be attributed to energetic masking and informational masking. If the target and masker have the same properties, even when the target and masker are processed in different peripheral channels (i.e., no energetic masking), the neurotypical people are still suffered from central, informational masking.

Objectives: This study investigated how autistic people are influenced by target-masker similarity and binaural (spatial) separation when there is no energetic masking between the target and masker.

Methods: Neurotypical and autistic participants were instructed to hear out the target among maskers in a two-interval forced choice experiment. The target was composed of pure tones at random frequencies that were within a protected spectral region, and it was sent only to the right ear. While the maskers were composed of pure tones outside the protected spectral regions, these pure tones either had random frequencies (condition 1 & 3) or had the same frequencies across time (condition 2 & 4). The maskers were either sent only to the right ear (condition 1 & 2) or to both ears (condition 3 & 4). Thresholds of the sound pressure level for the target to be heard out were measured by the 3-up-1-down staircase method.

Results: In the neurotypical group, the thresholds measured in condition 2 & 3 were significantly smaller than the threshold measured in condition 1. This observation is consistent with previous studies, which reveal the benefit from target-masker dissimilarity and binaural (spatial) separation. Nevertheless, in the autistic group, the thresholds in condition 1 were not significantly larger than the thresholds in other conditions. The thresholds in all conditions in the autistic group were similar to the thresholds observed in conditions 2, 3, and 4 in the neurotypical group.

Conclusions: The results show that when the spectral regions of the target and masker were not overlapped, the ability to hear out the target in the autistic group was not degraded by target-masker similarity. This observation supported the hypothesis that when autistic people process local information, they are less influenced by the distracting global information.

**140.093 93** The Communication Profile and Quality of Communication in Young Adults with Autism. W. Mitchell* and J. Volden, *University of Alberta*

Background:

Little is known about the overall communicative profile of high-functioning adults with autism spectrum disorder (HFASD) and even less about how listeners react to it. A variety of communication impairments have all been documented but results have been mixed across studies. Listeners judge communicatively-impaired individuals more negatively (e.g., as **less** likeable, employable) than those with typical communication but this issue has not been studied in adults with HFASD.

Objectives:

To compare (1) communicative profiles of 15 adults with HFASD to matched controls using a battery of communication measures and (2) naïve listener impressions of communicative quality. Performance on the Communication Checklist-Adult (CC-A) and the Non-Literal Language (NLL) and Pragmatic Judgment (PJ) subtests from the Communication Assessment of Spoken Language (CASL) is expected to reveal deficits in pragmatic skill, while difficulties in syntax or vocabulary on the Test of Adolescent and Adult Language – 4 (TOAL-4) may or may not be evident. We expect community listeners to judge communicative quality of adults with HFASD as poorer than controls.

Methods:

Participants, matched on age, performance IQs, schooling and gender, were given subtests from the TOAL-4 and the CASL and an informant completed the CC-A. Participants also completed a simulated "getting to know you" job interview with a professional recruitment consultant. To assess communication quality, 10 community listeners rated the 'quality' of communication, using a 7-point scale, in audio-taped interviews of 4 HFASD and 4 controls.

Results:

A MANOVA, with diagnostic group as IV and subtest scores for semantics, syntax and pragmatics as DVs. found significant group differences ($F(2, 27) = 18.01, \alpha < .05$) for pragmatics (NLL and PJ subtests) between the HFASD group (M=87, M=84, respectively) and the controls (M=106, M=100, respectively). Even so, scores were essentially within normal limits for the HFASD group. A MANOVA with diagnostic group as IV and CC-A composite scores (Structural Language, Pragmatic Skill, and Social Engagement) found significant differences ($F(3, 26) = 21.95$, Bonferroni adjusted $\alpha = .017$), between the HFASD (Ms = 7.4, 4.8, 2,8, respectively) and the controls (Ms=12, 10.6, 11.4). Mean quality ratings for the interviews of participants in the HFASD group (M=3.97, SD = 1.87)) were significantly different than average ratings of quality for the controls (M= 5.6, SD = 1.23; $t(67.5) = 4.57$).

Conclusions:

For these adults with HFASD, standard scores on the TOAL-4 and the CASL did not indicate impairment, but results from the CC-A detected pragmatic and social dysfunction. Whitehouse and Bishop (2009) note that impaired scores on 2 or more subscales of the CC-A indicate communication difficulties that influence everyday life . Importantly, everyday listeners rated the quality of communication in the simulated interviews of adults with HFASD as significantly poorer than controls. Thus, even subtle differences in quality can have a negative impact on conversational partners. If these findings hold true in our larger sample, it may help explain why adults with HFA sometimes fail to advance beyond a job interview, despite being well-qualified.

**140.094 94** The Effect of Developmental Status and Parental Acceptance of Emotion on Parenting Stress. H. N. Davis, B. J. Wilson*, J. Berg, T. Estrada, J. Sparrow and M. L. Zavertnik, *Seattle Pacific University*

Background:

Parents of children with ASD report more parenting stress than the general population (Steijn, Oerlemans, Aken, Buitelaar, & Rommelse, 2013). Furthermore, researchers have found parents exhibit more stress when parenting children with ASD than with typically developing (TD) children (Steijn et al., 2013; Hoffman, Sweeney, Hodge, Lopez-Wagner, & Looney, 2009). Research suggests parental acceptance and wellbeing are associated. Weiss and colleagues (2012) found parental acceptance of difficult cognitions and feelings surrounding

parent-child relationships mediated the relation between child problem behaviors and parent mental health. Acceptance of factors relating to caregiving may be an important variable in reducing risk for elevated stress and mental health concerns in parents of children with ASD.

Objectives:

The purpose of our study was to examine the influence of parental acceptance of emotion on parenting stress in parents of children with ASD and TD children. Parents with high acceptance of emotion appear comfortable with their child's emotion, empathize, and participate in the child's emotional experience without punishing or dismissing (Gottman, 1996). We hypothesized acceptance of emotion would buffer against elevated levels of stress common in parents of children with ASD.

Methods:

Our preliminary sample included 61 children ages 3:1 to 6:11 and their parents. Forty-two children (45.2% female) were TD; 19 children had a diagnosis of ASD (21% female). The study utilized a case-control format and measured children's verbal abilities using the *Differential Ability Scales II*(DAS-II; Elliot, 2007). Parental acceptance of sadness, anger and fear were coded from audiotaped responses to the Meta-Emotion Interview (MEI; Katz & Gottman, 1986). Additionally, parents completed the Parenting Events Questionnaire (Crnic & Greenberg, 1990) measuring parenting stress frequency and intensity.

Results:

A hierarchical regression analysis examined the influence of developmental status and acceptance of emotion on parenting stress. Child verbal ability, developmental status, and parental acceptance of emotion were entered in the first step and predicted significant variance, $R^2 = .20$, $F(3, 57) = 4.81$, $p = <.01$. An interaction term of developmental status and parental acceptance of emotion was entered in the second step. Significance of the interaction term was trending, $F(1, 56) = 3.52$, $p = .066$. Parents of children with ASD who reported high acceptance of emotion also reported significantly lower parenting stress than parents of children with ASD who reported lower acceptance of emotion. Parents of TD children had similar levels of parenting stress regardless of acceptance level. To increase the power of our analysis, we will continue data collection.

Conclusions:

Findings indicate acceptance of emotion is associated with lower parenting stress in parents of children with ASD. Greater acceptance may buffer against stress and discomfort experienced while caring for children with dysregulated emotions and behavior. Parental acceptance of emotion may be an important area for future interventions targeting stress and psychological wellbeing in caregivers of children with ASD. We plan to report data on a larger sample and hope to replicate our findings.

**140.095 95** The Effect of Spanish VS. Non-Spanish Bilingual Exposure on Expressive Communication Scores for Toddlers with Autism Spectrum Disorder. J. Berman*[1], B. Davis[1], C. Klaiman[2] and C. A. Saulnier[1], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*

Background:

Researchers have recently begun investigating the impact of bilingual vs. monolingual exposure on the expressive communication development of children with ASD. Most research has demonstrated a negligible difference in language development between the two groups (Valicenti-McDermott, et al, 2012; Hambly & Fombonne, 2011; Ohashi, et al, 2011), however some research has suggested that second-language exposure can be a predictor of lower expressive language scores among children with ASD (Chaidez, et al, 2012). As the percentage of bilingual speakers in the United States continues to rise, it is important to enhance our understanding of the effect of bilingual exposure on children with ASD, so that we may develop more informed recommendations to bilingual families on the benefits and drawbacks of multiple-language exposure.

Objectives:

This investigation builds off of the study by Chaidez and colleagues (2012), to investigate whether expressive language and non-verbal

communication skills vary among bilingually-exposed toddlers with ASD, particularly depending on whether the second language in addition to English is Spanish or another language. As our dataset expands, we will compare communication skills among individuals who are bilingually-exposed to English and additional languages, including Asian and European languages.

Methods:

Participants included a clinically-referred sample of 52 toddlers (40 males and 12 females) with a confirmed ASD diagnosis, consisting of 41 monolingually-exposed children and 11 children who are spoken to at least 10% in a secondary language in addition to English (8 in Spanish and 3 in another language). This is an ongoing study, and we expect to ascertain approximately 40 more English/Spanish bilingual toddlers and 20 English/other-language bilingual toddlers which will enable us to more effectively test across secondary language groups. The mean age for monolingual children was 23.63 months (SD=3.17) and the mean age for bilingual children was 23.27 months (SD=3.66). The measures used included a demographics questionnaire, the *Mullen Scales of Early Learning,* the *Vineland Behavior Scales, 2nd Edition, Survey Form,* and the *Communication and Symbolic Behavior Scales (CSBS)*.

Results:

Consistent with prior research, no significant differences between bilingually- and monolingually-exposed children were found on the Mullen and Vineland expressive language subdomains [$F(1,49)=.419$, $p=.520$] and [$F(1,50)=.454$, $p=.503$], respectively. However, contrary to Valicenti-McDermott and colleagues (2012), we did not find a significant difference between bilingually- and monolingually-exposed children's utilization of gestures as recorded by the CSBS Gestures subscale [$F(1,48)=.189$, $p=.666$]. We also found no significant differences between the Spanish and non-Spanish language groups on the Mullen expressive language subdomain [$F(2,48)=.271$, $p=.763$], Vineland expressive language subdomain [$F(2,49)=.227$, $p=.798$], or CSBS Gestures subscale [$F(2,47)=.095$, $p=.910$].

Conclusions:

Preliminary results of this study supported the outcomes of previous studies, finding no significant difference in expressive language scores between children with ASD exposed to monolingual and bilingual environments. These preliminary findings may offer important information for intervention, as many families and professionals struggle with the best course of speech and language treatment for bilingual families. Further examination following the introduction of the additional data will be beneficial to determine any within-group differences on expressive communication measures among the bilingually exposed children.

**140.096 96** The Impact of a Visualizing and Verbalizing Intervention on Language Ability in Children with Autism Spectrum Disorders. A. R. Lemelman*, D. L. Murdaugh, C. E. Crider, S. E. O'Kelley and R. K. Kana, *University of Alabama at Birmingham*

Background: Deficits in language comprehension have been widely reported in children with autism spectrum disorders (ASD). Such deficits generally range from lack of functional speech to difficulties in comprehension and discourse processing (Tager-Flusberg et al., 2005). Deficits in language result in variable reading profiles in individuals with ASD, the most common being that of poor comprehension despite adequate decoding skills (Nation et al., 2006). Improving reading comprehension in children with ASD is a challenging task. The *Visualizing and Verbalizing for Language (V/V)* Intervention program (Bell, 1991; Torgeson et al., 1999) targets visual imagery skills of children with language disabilities to help them improve both oral and reading comprehension.

Objectives: The goal of the present study was to investigate the impact of a 10-week intensive *V/V* language intervention on reading and language abilities in high-functioning children with ASD.

Methods: Children (ages 8-13 years) with ASD were randomly assigned to an Intervention group (n = 23) or Wait-List Control group (n = 18). Additionally, children with typical development (n= 26) were recruited as a control group. Children in the Intervention group received the *V/V* training, a one-on-one intervention that lasted 10 weeks (total = 200 hours of direct instruction). All children with ASD were tested on a variety of neuropsychological measures at baseline and at 10 weeks.

Results: (1) At baseline, the Intervention group had significantly lower scores than the control group on their reading comprehension ($t(47)=-6.24$, $p=.000$) on the *Gray Oral Reading Test-4* (GORT-4), receptive vocabulary ($t(47)=-2.43$, $p=.02$) on the *Peabody Picture Vocabulary Test-4* (PPVT-4), expressive vocabulary ($t(47)=-1.97$, $p=.05$) on the *Expressive Vocabulary Test-2* (EVT-2), and oral comprehension ($t(46)=-2.63$, $p=.01$) on the Oral Directions subtest of the *Detroit Tests of Learning Aptitude-2* (DTLA-2); (2) After 10 weeks, the Intervention group did not differ from the control group on their scores on the PPVT-4, EVT-2, or DTLA-2. The Wait-List Control group did not show this pattern of results at pre- or post-testing; and (3) The Intervention group significantly improved their reading comprehension scores on the GORT-4 following intervention ($F(1,21)=15.06$, $p=.001$, partial eta squared=.418).

Conclusions: The language intervention in this study was designed to use nonverbal sensory input to develop oral and written language comprehension, establish vocabulary, and develop higher order thinking skills. Our findings revealed that following intervention, children with ASD improved their receptive and expressive vocabulary, as well as oral comprehension to the level of typically developing control children. The intervention group also showed an improvement in their comprehension from first session to the second. Overall, our findings suggest that the *V/V* program appears helpful in improving vocabulary and oral comprehension abilities in children with ASD. More research, with larger samples, is needed to further establish the effectiveness of this program on reading comprehension abilities in children with ASD.

**140.097 97** Training Parents in Jasp-EMT: Using Empirical Benchmarks to Evaluate Generalization and Maintenance of EMT Strategies.

J. D. Bryant*[1], J. Heidlage[1], A. P. Kaiser[1] and C. Kasari[2], (1)*Vanderbilt University*, (2)*UCLA*

Background: Implementation fidelity in parent-implemented early communication interventions is essential to ensuring effects of children's language outcomes. Although many studies report changes in parent use of trained strategies, few compare parent performance to empirical benchmarks for effective implementation. Fidelity benchmarks provide a standard for evaluating parent implementation beyond demonstrating changes in use of strategies from pre to post-treatment. JASP-EMT (Joint-Attention, Structured-Play, Enhanced Milieu Teaching) is a social communication intervention that blends EMT (Enhanced Milieu Teaching) with JASPER (Joint-Attention, Structured-Play, Engagement, Behavior Regulation), two interventions that have been found effective in improving communication and related skills in young children with autism. Because interventions employing both therapists and parents may help children accelerate their language development and use, determining the extent to which parents can learn, generalize and maintain use of the strategies is important.

Objectives: The purpose of this study was to evaluate effects of training parents in the EMT component of the JASP-EMT intervention by examining parent fidelity of six intervention strategies from pre-intervention to post-intervention and maintenance of these skills at the 3-month follow-up testing point: 1) matched turns; 2) responsiveness; 3) expansions; 4) target level language; 5) time delays; and 6) milieu prompting episodes. Parent strategy use was compared to empirical benchmarks for effective EMT implementation.

Methods: The participants in this study were the parents of 20 minimally-verbal children with autism ages 5-8 who received parent training as part of a larger randomized trial of JASP-EMT. Child participants received 1-hour intervention sessions twice per week with a therapist for a total of 48 sessions. Parent training occurred in two phases. During phase 1 (24 sessions), parents observed the sessions while children received the intervention from a therapist. During phase 2 (24 sessions), parents were trained individually and practiced with the child while receiving coaching and feedback. Parent fidelity in EMT strategy use was measured during each intervention session; generalization was measured in Caregiver-Child Interaction sessions (CCX) administered at post-intervention (session 48) and maintenance was measured in CCX sessions at the 3-month follow-up.

Results: Parents significantly improved their use of all six strategies from pre-intervention to post-intervention. They generalized strategy use to the CCX and maintained use at the follow-up. Five of six strategies were generalized and maintained at or near benchmark levels: matched turns (criterion=50%; 56.4% post-intervention, 55.7%

follow-up), responsiveness (criterion=80%; 85.7% post-intervention, 84.8% follow-up), expansions (criterion=40%; 45.1% post-intervention, 44.7% follow-up), target level language (criterion=50%; 46.9% post-intervention, 48.2% follow-up), and time delays (criterion=80%; 73.9% post-intervention, 73.1% follow-up). Percentage correct milieu episodes was below criterion at post-intervention and follow-up (criterion=80%; 29.3% and 30.0%, respectively).

Conclusions: Results indicate parent training was highly effective for teaching parents EMT strategies to support child communication, although additional training may be required for long-term use of milieu episodes. Future studies should focus on improving generalized performance by training across settings to ensure parents have skills for supporting emerging communication skills. Given the strong positive outcomes in this study, future studies should examine the usefulness of empirical benchmarking for parent use of intervention strategies.

**140.098 98** What's Your Story: Narrative Language and Cognition Among School-Aged Children with ASD. G. Greco, C. Sonners, N. Nayudu and S. Faja*, *University of Washington*

Background: Among individuals diagnosed with autism spectrum disorder (ASD), a delay or diminishment of the development of language and communication is a core feature of the disorder. Children with ASD also have more difficulty with tasks used to measure verbal working memory when compared to typically developing individuals (e.g., Gabig, 2008; Joseph et al., 2005), though findings have been mixed (e.g., Williams et al., 2005). Among typically developing children, one aspect of language that may be particularly related to verbal working memory is narrative ability (Gabig, 2008). Previous work has shown that verbal working memory relates to communication skills in children with ASD (Joseph et al, 2004). Although research has documented differences in the narrative ability of children with ASD (Capps, Losh, & Thurber, 2003), there have been no studies that have examined the role of working memory in the narratives of children with ASD.

Objectives: To explore whether parent report of narrative ability differed between children with ASD and children with typical development (TD). To evaluate whether groups differed on an observational measure of narrative ability. To investigate whether narrative ability corresponds to working memory (WM) within the group with ASD.

Methods: Data collection is ongoing with data currently available for 66 children. Participants are 6 to 11 year-olds with ASD and TD – all with average or above average IQ. Working memory was measured using the Children's Memory Scale Numbers subtest and by parent report from the Behavioral Rating Inventory of Executive Function (BRIEF). Composites of individual items related to narrative ability were created for both the Expressive and Interpersonal Relationships (IR) subtests of the Vineland-II parent interview. Narrative ability is also being coded from a speech sample obtained during the Autism Diagnostic Observation Schedule using Reilly, Klima, and Bellugi's (1991) narrative coding scheme.

Results: Preliminary results showed that groups differed on the Vineland Expressive composite, $t(63)= -6.64$, $p < .001$, Vineland IR composite, $t(63)= -6.29$, $p < .001$, a combination of both Vineland composites, $t(63)= -7.00$, $p < .001$, and BRIEF WM, $t(60)= 5.57$, $p < .001$, though no differences were found with CMS scores. This suggests that there are differences in narrative ability between the two groups, though results about working memory are mixed. Among children with ASD, BRIEF WM scores related to the Vineland Expressive composite, $r(34) = -.40$, $p = .02$. No correlation was found between CMS scores and any of the Vineland composites. Results of behavioral coding and the relation between observed narrative ability and cognitive function will also be presented.

Conclusions: Children with ASD differed from those with TD on Vineland composite measures of narrative and on parent report of working memory, but not during a behavioral working memory task. Among the group with ASD, preliminary results provide some evidence for a relation between working memory and narrative ability. Behavioral coding will provide a richer analysis of narrative ability and, therefore, may provide additional information about the relation of working memory to narrative abilities.

## 141 Services

**141.099 99** Autism in Bangladesh: Window for Stigma Removal. M. Rabbani[1], H. U. Ahmed*[2], M. Mannan[3], W. A. Chowdhury[4], M.

F. Alam[4] and T. Hossain[5], (1)*Bangladesh Association of Psychiatrists*, (2)*National Institute of Mental Health (NIMH) Bangladesh*, (3)*CNAC-BSMMU*, (4)*NIMH*, (5)*BIRDEM Hospital*

Background: Bangladesh is a South East Asian developing country with moderate literacy rate with three leveled health care delivery system. Most of the citizens of Bangladesh live in rural area and devoid of modern approach of technology and also having stigma on health care seeking attitude. Especially the rural person depends on the traditional and religious healers for their behavioral disturbance like autism and other mental condition. There is a common false belief that the autism and other mental disorders are caused by ill spirits and need some measure other than medication. A study revealed more than 50% rural people have faith on traditional healers. This false belief and stigma act as a barrier to promote scientific management for the mental disorders including autism. Though there are a lot of community clinics in grass root level and structured level wise health centers exist the people are more interested to take treatment from spiritual healers.

Objectives: To change the health seeking behavior of rural people need to create general awareness and mitigate stigma by the advocacy program. Before create the general awareness we need general education and inclusion of autism related topics in school curriculum. Training for the general physicians and other health professionals is a vital component because they are the first contact for the all people in health service. Mass awareness can be creating by using the mass media and using traditional folk songs and drama. There is very important issue to trained the traditional healers and provide them the scientific knowledge about autism and other neurodevelopmental disabilities. To provide ideal service and increase public awareness and reduce stigma the local opinion leaders and religious leaders also need to be trained. Within a specific interval the process evaluation should be conducted.

Methods: Country will divided into multiple clusters and from each clusters a significant number of primary care physicians, traditional healers, opinion leaders and religious leaders will be included into the training. By using the existing health facilities and the manpower the training will be conducted in tertiary care institutes like National Institute of Mental Health (NIMH) and Center for Neurodevelopment and Autism for Children (CNAC). Training modules and manual should be in native language and folk songs and drama also used for training.

Results: N/A

Conclusions: Social stigma and lack of awareness is the main barrier to provide appropriate service for autism spectrum disorders. By generating public awareness through training, advocacy, cultural activities and using the mass media the current scenario should be changed. Bangladesh will be create an example for the low resource countries that how to develop coordinated multidiciplinary services and social inclusion of the people with autism.

**141.100 100** "It's like a Little Secret World:" the Experience of Military Families with a Child with ASD. J. M. Davis* and E. H. Finke, *Pennsylvania State University*

Background: Military families are an underrepresented group in the ASD literature, despite the number of military dependents with a diagnosis of ASD reaching approximately 23,500 (Tricare, 2011). Although there have been no peer-reviewed studies about military and ASD related topics to date, some reports and parent guidelines from the Department of Defense (DOD) have outlined some possible challenges military families with a child with ASD may experience (e.g., OAR, 2010; DOD, 2011a; National Council on Disability, 2011). These documents indicate issues such as greater emotional reactions, reduced continuity of care, changes in service eligibility across state boundaries, and access to appropriate educational programming as potential effects for children with ASD and their families as a result of military separation and relocation (OAR, 2010; National Council on Disability, 2011). Given the unique challenges families encounter with having a child with ASD and the unique stressors for military families, military families who also have a child with ASD may have experiences that differ from either group.

Objectives: To determine the therapeutic experience of military families with a child with ASD

Methods: This study used a qualitative design with semi-structured interviews. Since research

on military families with a child with ASD is very limited, a qualitative methodology is needed to understand and describe their experiences so appropriate next steps can be implemented. Qualitative methodologies are used when information about a topic is limited (Morse & Field, 1995) and when the purpose of the study is to describe experiences by generating themes, identifying trends, and constructing theories based on the perception of events (Meline, 2006). The interview questions were generated through a review of the literature on the diagnostic and treatment process for families of children with disabilities and research on military families. The interviews were conducted via online video calling programs (e.g., Skype) and lasted approximately one hour. Each interview was audio recorded. The completed interviews were transcribed verbatim, with all identifying information removed, and were analyzed using a six step process adapted from grounded theory (Charmaz, 2006; Charmaz & Henwood, 2008) and focus group analysis techniques (McNaughton, Light, & Groszyk, 2001; Vaughn et al., 1996). The purpose of the analysis process was to determine themes and subthemes common across the participants. Point-by-point reliability and Cohen's kappa were calculated to be 89% and .86, respectively.

Results: Data analysis is currently on-going, but preliminary results suggest military families experience barriers, supports, negative and positive impacts related to therapeutic programming for their child with ASD.

Conclusions: Data analysis is currently on-going, but conclusions may impact clinical service providers, military programming and providers, and laws and policies.

**141.101 101** Autism in Bangladesh: Current Scenario and Future Prospects. H. U. Ahmed*[1], M. Mannan[2], M. F. Alam[3], T. Hossain[4], N. F. Chowdhury[5], W. A. Chowdhury[3] and M. Rabbani[6], (1)*National Institute of Mental Health (NIMH) Bangladesh*, (2)*CNAC-BSMMU*, (3)*NIMH*, (4)*BIRDEM Hospital*, (5)*BSMMU*, (6)*Bangladesh Association of Psychiatrists*

Background: Bangladesh is a developing country from South East Asia having population of 167 million. According the World health Organization supported survey 2009 there are 0.84% children are suffering from Autism Spectrum disorders. Against this magnitude of disease burden only 200 psychiatrists, and limited number of other l health professionals are serving the nation. Bangladesh has very well developed three tired health care delivery system but the service for autism is available only at the upper level of the pyramid. The community living at the rural and semi urban areas is devoid of appropriate services for their ward with Autism. To minimize this problem and provide an integrated service for all, the country needs to be incorporated the care for autism from the bottom of health service system, which is at the primary health care. It is not possible to increase the number of skilled health professionals overnight, so this present project can create a group of skilled manpower who will be able to provide primary service to the children with autism and advice to the parents accordingly.

Objectives: To provide effective and better services for children with autism through primary health care by using existing resources and manpower. To train primary health care physicians as they become skilled to handle (screening, diagnosis and management) Autism and referred to next level when necessary. To reduce treatment gap and decrease the treatment cost Autism. To be establish the e-autism service by using web camera and internet.

Methods: For the capacity building the country need to trained the primary health care professionals who are working in 13000 community clinics. A door step health care service system exists, just need to incorporate there the Autism related services. There are lack of multidisciplinary approach in Autism services; need to make a common framework for pediatrician, psychiatrists, psychologists and other support service staffs. Plan to make a national guideline for autism management. Need intensive but short term training on autism diagnosis and management for field level physicians. Training materials include manual for training consisted several modules and multimedia will be used. Beside the training a cell phone and internet based web camera will be placed in every community health clinics and trained physicians can contact with the centrally placed autism experts 24 hour through a hot line

Results: The primary care physicians will be able to screen, assess, diagnose and manage primarily Autism Spectrum Disorders. They would be able to refer the children to the next step rationally. The effectiveness of training will be reflected in

the attitude, assessment and management plan of the primary health care physicians. Referral and back referral system will be established.

Conclusions: 'When there is no way, create one', with this proposition, country will able to deliver better services for Autism to the community where the number of health professionals and resources are inadequate. By this notion, Bangladesh will change its autism scenario and set up an example for South East Asian countries as well as other developing countries.

**141.102 102** "You Are the Voice of Your Child, If You Don't Speak up, No One Will Hear Your Son": Latino and African American Parents' Perceptions on Access to Care for Children with Autism. K. Kubicek*[1], M. Robles[1], K. Smith[2], L. Richard[2] and M. D. Kipke[1], (1)*Southern California Clinical and Translational Science Institute*, (2)*Children's Hospital Los Angeles*

Background: While there is no evidence to suggest that the odds of an autism spectrum disorder (ASD) diagnosis is dependent upon family characteristics such as race/ethnicity, income or education, research examining the diagnosis of autism has found disparities in diagnosis and access to care among Latino and African American children. Developing programs to address these disparities is important, as early diagnosis is critical for improved health outcomes for children with ASD

Objectives: The current study was designed to better understand the challenges that Latino and African American parents of children with autism experience in receiving a diagnosis and treatment. The study was designed to address the following research questions: 1) What is the process parents go through to receive their child's autism diagnosis?; and 2) How do parents describe/characterize their experiences in accessing services for their children? This study takes a mixed methods approach to better understand the experiences of parents in accessing services for children with autism. This approach is important as it has the potential to identify intervention modalities that are culturally appropriate for the target population.

Methods: A total of ten focus groups were convened with 56 African American and Latino parents. Focus groups were organized by race/ethnicity and language preference. A short survey was also completed at the end of each focus group. Focus groups were facilitated by a bilingual team member and were digitally recorded and transcribed.

Results: Overall, parents reported low levels of knowledge about ASD and related services when their child was first diagnosed. The biggest service gaps when considering perceived need and access to care were found in Floor time, family therapy and applied behavioral analysis. Qualitative data indicate parents encountered community physicians who did not take their concerns about their child's development seriously. Parents also reported: cultural barriers such as reticence to question a doctor's judgment, stigma around a mental health issue, lack of family support, reticence to talk with outsiders about their child's diagnosis and language. In addition, parents described a pervasive perception that higher income and/or White families receive more and better services. They also described a confusing service system that was difficult to navigate.

Conclusions: Obtaining an ASD diagnosis can be a stressful and protracted experience for many Latino and African American parents. Parents reported numerous challenges navigating the service system and seemed to rely more on other parents for assistance and support than service providers. Developing a health navigation model with trained parents/community health workers/*promotores* may be a novel way to provide parents support in navigating the service system. Recommendations for policy changes as to how ASD support services are delivered are also discussed in order to have a more equitable service system.

**141.103 103** A Behavioral Parent Training Model for Children with Autism Spectrum Disorders: Preliminary Outcomes. A. A. Fulton*, C. Delfs, A. Baker, H. Robinson and C. Furlow, *Marcus Autism Center, Children's Healthcare of Atlanta and Emory University*

Background: Intensive behavioral interventions are often effective at reducing maladaptive behavior. However, they can often be costly and procedural fidelity following training sessions can be lacking (Jacobson, Mulick, & Green, 1998). A potential alternative is behavioral parent training (BPT) with a focus on teaching general behavior management strategies based on the principles of applied behavior analysis (ABA). These programs are relatively inexpensive, shorter in duration than other intensive interventions, and place

emphasis on the importance of caregiver involvement, training, and education (Serketich & Dumas, 1996).

Objectives: The purpose of the current investigation was to examine the effects of a BPT program on problem behavior in children with autism.

Methods: Participants for this study included 31 families consisting of at least one caregiver with a child 2-9 yrs old diagnosed with an autism spectrum disorder completing a BPT program. Sessions were conducted in the community setting (i.e., caregiver's home). Each family participated in a 2-hour session, once a week, for a minimum of 9 weeks of a 12-week admission. The problem behavior portion of the Scales of Independent Behavior-Revised (SIB-R) was administered by parenting counselors during the initial intake session and final session to measure problem behavior. The SIB-R ratings provided by caregivers reflected the frequency and severity of the following problem behaviors: hurtful to self, hurtful to others, destructive to property, disruptive behavior, unusual or repetitive behavior, socially offensive behavior, withdrawal or inattentive behavior, and uncooperative behavior. Raw scores from parent ratings were used to calculate the following indices: internalized maladaptive index (hurtful to self, unusual/repetitive habits, withdrawal/inattentive behaviors), asocial maladaptive index (socially offensive behaviors, uncooperative behaviors), and externalized maladaptive index (hurtful to others, destructive to property, disruptive behavior).

Results: Generally, mean SIB-R index scores improved from pre-admission to post-admission. Data were analyzed using within-subjects repeated measures ANOVA to determine if SIB-R scores were statistically significant across all indices.

Conclusions: The results suggest general education and targeted behavioral parenting skills taught throughout the BPT are associated with decreased frequency and severity of problem behaviors. However, these findings are tentative as they are based solely on parent report and responses scored on the SIB-R.

**141.104 104** Access to Care: Familial and Cultural Variables Associated with Limited Service Access in Individuals with ASD.

S. Grunewald*[1], L. Kraus[1], N. Forburger[1], S. Youngkin[1], R. Loftin[1] and L. Soorya[2], (1)*Rush University Medical Center*, (2)*Rush University*

Background: Although there are a wide variety of treatment options that can positively impact a child with Autism Spectrum Disorder (ASD), accessing necessary services can be difficult. In addition to variables assessed in previous literature, such as overall availability, contact accessibility, appointment accessibility, and geographic accessibility (Hall, Lemak, Steingraber, & Schaffer, 2008), we must also explore economic barriers, familial stressors, and cultural implications.

Objectives: To provide preliminary data on factors influencing access to care from a survey of parents/caregivers of individuals with ASD, other neurodevelopmental disorders, and childhood psychiatric disorders.

Methods: Data was collected from 469 respondents in total ranging from infancy to 50 years of age. Of those respondents, 243 identified an ASD diagnosis according to the DSM-IV-TR, which includes autism, Asperger's disorder, and pervasive developmental disorder. Examples of diagnoses in the comparison sample included Speech and Language Disorders, Mental Retardation, Obsessive Compulsive Disorder, and Oppositional Defiant Disorder. In addition to demographic questions regarding race, education level, and income level, questions focused on the treatments being sought, payment type (i.e., public insurance, private insurance, or self-pay), and services covered.

Results: Data was collected from 469 respondents in total ranging from infancy to 50 years of age. Of those respondents, 243 identified an ASD diagnosis according to the DSM-IV-TR, which includes autism, Asperger's disorder, and pervasive developmental disorder. Examples of diagnoses in the comparison sample included Speech and Language Disorders, Mental Retardation, Obsessive Compulsive Disorder, and Oppositional Defiant Disorder. In addition to demographic questions regarding race, education level, and income level, questions focused on the treatments being sought, payment type (i.e., public insurance, private insurance, or self-pay), and services covered.

Conclusions: Accessibility to interventions is an absolute imperative; however, the results indicate that families are not able to utilize necessary treatments due to cost, familial stressors, and cultural/ethnic differences.

**141.105 105** Advocate with Autism Resources and Education (AWARE): A Training Program to Increase Community Awareness and Acceptance of Persons with Autism Spectrum Disorders and Their Families. L. S. Castriota*[1], M. J. Segall[2], T. Thomas[1] and J. F. Cubells[1], (1)*The Emory Autism Center*, (2)*Emory Autism Center*

Background:

Navigation through community situations is often challenging to the increasing number of individuals and families who cope daily with Autism Spectrum Disorder (ASD). The need for community awareness of and sensitivity toward individuals with ASD and their families is a growing imperative if such persons are to succeed socially, occupationally, educationally, and achieve good health, happiness and dignity.

Objectives:

To develop and evaluate a program aimed at helping institutions and typical individuals comprising the larger community to understand individuals with ASD and their families, and thereby improve their abilities to welcome, accept, and communicate more effectively with persons affected by ASD.

Methods:

*Advocate With Autism Resources and Education* (AWARE) educates people in key community institutions about ASD. Such establishments receive materials indicating to the public that they have participated in such training. The program consists of a comprehensive training module, regularly scheduled follow-ups of participants with the instructor, and opportunities for individuals with ASD to provide anonymous feedback on the site where training occurred. All AWARE participants complete a pre and post-test, before and after the training.

Results:

Recently, 35 individuals at a major international airport received AWARE training. Participants included staff of several airlines, officers of the Federal Transportation Safety Administration, and customer service personnel of the airport itself. Feedback on the experience by participants has been consistently positive. We are now tracking the anonymous feedback of persons with ASD and their families. Several additional trainings have been conducted at other institutions and businesses, for a total of 70 AWARE-trained individuals in the greater Atlanta region.

Conclusions:

Program feedback suggests that AWARE, a formal education program aimed at increasing community acceptance and inclusion of persons with ASD, has been enthusiastically received by participants thus far. We will present data on the scope of this growing initiative, and on feedback from persons with ASD and their families.

**141.106 106** An Autism Researcher's Toolbox for Community Engagement. A. Yusuf*[1], K. Shikako-Thomas[2], S. Prasanna[1], C. Ruff[3], M. Fehlings[3] and M. Elsabbagh[1], (1)*McGill University*, (2)*McMaster University*, (3)*Krembil Neuroscience Centre, Toronto Western Hospital*

Background: The last decade has seen significant growth in scientific understanding and in global public awareness of autism. Ideally, the best available research is developed within the context of the characteristics and values of the beneficiaries of such research; moreover it is reflected in policies set to improve the lives of those beneficiaries.

A key goal in community engagement is to direct the mainstream autism research agenda to meet the immediate needs and priorities of diverse stakeholders, i.e. families affected by autism, health practitioners and researchers in autism, etc. While there exist models describing the process through which knowledge generated from research impacts attitudes, practices, and policies, there is still little empirical data in autism research regarding such engagement and more importantly, how to measure its impact.

Objectives: Our aim is to highlight engagement models as they apply to autism research and to illustrate their utility in identifying knowledge gaps and stakeholders' priorities using two case studies.

Methods: Together, the INVOLVE model, CIHR's Integrated Knowledge Translation framework, and the K* movement endorse the notion that

knowledge is more likely to be useful, applicable, and impactful if the beneficiaries of research are engaged in the research process. They also advocate a continuum of responsibilities of researchers ranging from responsible communication of research to executing purposeful research driven by needs and priorities of stakeholders other than researchers themselves.

To illustrate the utility of these theoretical models, we report on two case studies of stakeholder engagement focused on identifying knowledge gaps and future research priorities in autism. Attendees in our first case study were Canadian community workers who support families affected by autism to understand the condition, seek appropriate professionals and services, and obtain moral and emotional support. The second case study included members of the International Society for Autism Research i.e. clinicians, researchers, and community advocates in autism. Attendees were divided into breakout groups of 10-12 participants and provided guiding questions. A facilitator was appointed for each group to ensure the discussion was focused and inclusive. All attendees reconvened for a second session wherein leaders of the breakout groups presented a summary of their discussion and received input from other groups.

Results: Both case studies highlighted the need to integrate families and community partners in dialogues surrounding research. Also prominent across both studies was for tailored knowledge to support caregivers in becoming active and empowered participants in care for those affected by autism. Participants identified that models of care that effectively consider both the context of application, along with the facilitators and barriers to implementing best practices, were lacking. The latter must include evaluation of existing and anecdotally successful models of care in diverse communities.

Conclusions: The case studies illustrate that information generated from research is indeed relevant and critical for knowledge users in the community. Moreover, simple and systematic methods can support the translation and uptake of knowledge in diverse communities, therefore enhancing engagement with research and bridging research findings with immediate community needs.

**141.107 107** Assessing Family Outcomes of Early Intervention: Utility of Items Specific to Families of a Child with an Autism Spectrum Disorder.

B. Elbaum*[1], D. M. Noyes-Grosser[2], K. Siegenthaler[3], R. G. Romanczyk[4], R. N. Cavalari[5], R. L. Carter[6], A. L. Barczykowski[6] and C. Zopluoglu[1], (1)*University of Miami*, (2)*Bureau of Early Intervention, New York State Department of Health*, (3)*New York State Department of Health*, (4)*State University of N.Y. at Binghamton*, (5)*State University of NY at Binghamton*, (6)*State University of New York at Buffalo*

Background: The mission of state early intervention (EI) programs under IDEA is to provide services and supports to both children 0-3 with developmental delays and their families. Since 2005, states have been required to report on families' perceptions of the extent to which EI helped the family achieve desired family outcomes. Families of a child with an autism spectrum disorder ("ASD families") may have specific needs that are not addressed by currently used outcome measures.

Objectives: To compare factor structures and scores associated with responses of ASD and non-ASD families to two sets of items inquiring about the helpfulness of EI to families served. Using Concept Mapping, one set of items was developed with families of children with a range of developmental delays, the other set with families of a child with an ASD.

Methods: 134 ASD families and 75 families of a child with a developmental delay other than an ASD responded to a survey on the impact of EI services in New York. All survey items had the same 6 response options, ranging from "Very strongly disagree" to "Very strongly agree." The 86 family-focused items to which all participants responded included 35 "general items" developed with stakeholder groups representing families of children with a variety of developmental delays, e.g., "EI services helped me and/or my family understand how to change what I'm doing to help my child as he/she grows," and 51 "ASD items" developed by ASD-focused stakeholder groups, e.g., "Early intervention services helped me and/or my family learn how to explain my child's unusual behaviors to others." Single- and multiple-factor models were fit to the survey response data for ASD and non-ASD families, separately, and for the general items and ASD items, separately. Additional analyses examined differences between ASD and non-ASD families in

terms of mean item scores, item difficulty parameters, and item factor loadings.

Results: For both ASD and non-ASD families, for both the general and ASD items, a 1-factor solution showed good fit to the data, GFIs > .982. Increases in GFI for the multi-factor models were exceedingly small. Comparing item factor loadings for ASD and non-ASD families, the congruence coefficient was .993 for the general items and .994 for the ASD items, indicating high similarity of factor structures across the two groups of respondents. Both mean item scores and IRT item difficulties were highly similar across the ASD and non-ASD families.

Conclusions: No meaningful differences were found between ASD and non-ASD families in their responses to sets of general vs. ASD-focused items addressing the extent to which EI services helped families to achieve desired family outcomes. The findings suggest that a common set of items can be used with both ASD and non-ASD families to report on their perceptions of the helpfulness of EI to their family. Future analyses will address the range of perceived EI impact *within* each group in order to better understand how variables such as type and intensity of services provided affect family outcomes of EI.

**141.108 108** Autism Comes to the Hospital: Perspectives of Child Life Specialists. P. Burnham Riosa*[1], B. Muskat[1], D. B. Nicholas[2], W. Roberts[3], K. P. Stoddart[4] and L. Zwaigenbaum[5], (1)*The Hospital for Sick Children*, (2)*University of Calgary*, (3)*University of Toronto*, (4)*The Redpath Centre*, (5)*University of Alberta*

**Background**: Children with Autism Spectrum Disorders (ASD) often have complex health needs and therefore are likely to visit a variety of health care settings, including acute care hospitals. Pervasive social, communication, behavioral, and sensory challenges associated with ASD are likely to be amplified in a hospital setting. Given these difficulties, it is important to understand the ways in which health care providers can appropriately care for these vulnerable patients.

**Objectives**: Child Life Specialists are pediatric health care professionals trained to help children cope with the social and emotional aspects of the hospital experience, especially through play-based interventions. In a previous investigation, Child Life Specialists were generally touted as helpful health care providers through a series of in-depth interviews with children with ASD, their parents, and other health care providers. Therefore, the purpose of the current study was to understand the unique perspectives of Child Life Specialists who provide hospital care to pediatric patients with ASD in the hospital. The ultimate objective of this study is to use these findings to inform best practices throughout the hospital for child patients with ASD.

**Methods**: Two focus groups were conducted with Child Life Specialists ($N$ = 21) at a large urban Canadian pediatric hospital. Participants described their experiences working with children with ASD in the hospital setting, strategies they found helpful or unhelpful, and their recommendations to improve patient care.

**Results**: Findings from our focus groups revealed that given their developmentally-focused training, Child Life Specialists perceived themselves to be well-equipped to provide highly competent care to pediatric patients with ASD. Participants reported listening to and communicating with parents openly for suggestions on how to provide appropriate support given his or her child's specialized needs. Participants recognized that parents were often strong advocates for their children, and therefore supported parents regarding advocacy issues as needed. Overall, Child Life Specialists reported a variety of skills, strategies, tools, and resources they use in supporting children with ASD who are hospitalized. Participants also stressed the importance of a strong multidisciplinary team and the need to recognize Child Life Specialists' valuable role in supporting these patients proactively, before challenges arise.

**Conclusions**: Results from our previous investigation of the experiences of pediatric patients with ASD who were hospitalized revealed that health care providers wanted specialized expertise regarding ASD and perceived that as an important component of building competence to appropriately support these patients. However, findings from this study revealed that Child Life Specialists already possess many of the skills, tools, and resources to appropriate support the special needs of these children. Child Life Specialists provided their perspectives of the hospital experiences of children with ASD and their families. Participants' recommendations from this study have been used to further refine

family- and staff-friendly resource toolkits that will be implemented at this hospital in the near future.

**141.109 109** Awareness on ASD Among Young Parents. R. Hock*, B. McKeever, R. McKeever and Z. Yu, *University of South Carolina*

**Background:** Recent estimates show that one in 88 children is diagnosed with Autism Spectrum Disorder (ASD). Research has established that interventions such as Applied Behavior Analysis, when delivered in the early years of a child's life, can lead to dramatic improvements in communication, achievement and adaptive behavior skills. However, family access to these interventions is dependent on the early identification and diagnosis of ASD. Parents play a central role in identifying signs and symptoms of ASD in their young children. Their knowledge of ASD signs and symptoms may contribute to their ability to identify developmental concerns and seek professional help. For this reason, organizations such as the CDC and Autism Speaks have launched campaigns to increase ASD awareness among parents. Despite these large-scale efforts, the authors were unable to find empirical research about ASD awareness among parents of young children. It is important to understand the factors that contribute to ASD awareness among young parents in order to guide future education and public communication efforts.

**Objectives:** The objective of this study is to explore the factors that contribute to ASD awareness among parents of young children in the general public. In particular, we will examine parent characteristics such as age, length of parenthood, race, education status, and personal involvement with the issue of ASD.

**Methods:** An online survey was distributed through Amazon's Mechanical Turk (MTurk) to parents (N=497) who have a child 2-years or younger (who do not have a child with ASD). ASD awareness was measured using an 18-item instrument comprised of ASD symptoms and other challenging child behaviors. Participants indicated whether each item was a symptom of ASD. Involvement, defined as the degree of personal connection or attachment to the issue, was measured using three Likert-type items ($\alpha$=.767). Multiple regression was used to address the study aims.

**Results:** Regression results indicate that the model significantly predicts ASD awareness among parents of young children, $R^2$=.085, F(5, 496)=9.266, p<.001. Higher levels of education among parents ($\beta$=.092, p=.038) and ASD Involvement ($\beta$=.226, p<.001) were associated with increased ASD awareness, while being Asian ($\beta$=-.211, p<.001) was associated with lower ASD awareness. Length of parenthood, and membership in other racial groups were not significantly associated with ASD awareness.

**Conclusions:** Findings from this national cross-sectional study suggest that parent demographic characteristics and personal involvement with ASD contribute to their awareness of ASD signs and symptoms. These findings are an important first step in identifying differential awareness levels and information needs among young parents and may be used to guide public communication efforts. In particular, awareness appears to be lower among Asian parents and parents with lower levels of education. Implications for future research, practice, and policy will be discussed.

**141.110 110** Can We Increase Teachers Self-Efficacy to Teach the Autism Curriculum?. K. Johnsen*, C. Flint and J. Salt, *HAVE Dreams*

Background:

As teacher self-efficacy has been related to many positive benefits in the classroom, research has begun to look at self-efficacy effects during teacher training. General self-efficacy measures appear to make little contribution. *Autism specific* self-efficacy measures are currently being developed and validated. The Autism Self-Efficacy Scale for Teachers (ASSET; Ruble et al., 2013) holds promise and integrates well with our training model.

Our training program is a state-wide, intensive training based on structured teaching principles. The week long, interactive training provides an opportunity to receive in-vivo supervision and feedback from experienced trainers. Through lectures and hands-on construction of visual supports and materials, participants create a classroom, work with children with ASD and teach the autism curriculum.

To further study the effects of our training model, we added the ASSET measure to our evaluation protocol.

Objectives:

This study investigated the effectiveness of the training model to increase teachers competence in delivering the autism curriculum. The study addressed:

(i) teacher change in self-efficacy pre and post training.

(ii) the relationship of teachers self-efficacy to professional experience prior to training.

Methods:

Participating teachers (n= 46) who attended the hands on 5 day training workshop, completed the ASSET questionnaire pre and post training. ASSET is a 30-item self-report measure designed to assess ASD specific knowledge and skills. Each question is rated on a 1-100 scale.

To determine if individual variables affect self-efficacy, teachers also provided information related to their educational qualifications, number of years teaching, and experience with students with ASD.

Results:

i) T-test revealed that for the whole group, there was a significant ($p<.001$) increase in ASSET scores pre and post training.

ii) Baseline ASSET scores were divided by the mean score to create high and low self-efficacy groups. To determine the effect of prior experience on teacher self-efficacy, data was entered in a logistic regression model with group membership (high and low self-efficacy) as the dependent variable, and lifetime number of ASD students, educational level, and years teaching as covariates. There were no significant effects of professional experience predicting self-efficacy group membership.

Conclusions:

These results indicate the effectiveness of our training program. By attending the training, teachers increased their confidence in their ability to teach the autism curriculum, at any level of ability, to individuals with ASD. Teachers in both the low and high self-efficacy groups increased their scores over the training period.

Furthermore, teacher's self-efficacy for autism strategies appeared to have little relationship to their prior professional experience, experience with autism or their educational level. This has important implications for training teachers. Even teachers who have many years teaching experience, or who have taught many students with ASD, can increase their autism teaching self-efficacy by attending an intensive training. Our follow-up study will determine if self-efficacy predicts *implementation* of specific strategies in the classroom following training.

**141.111 111** Empowering Self-Advocacy: A Participatory Action Peer-Mentor Model. D. Bublitz*[1], T. Cintula[2], Y. Chen[2], A. Donachie[2], A. Schimmel[2], V. Wong[2], D. Pisana[2], R. Obeid[1], P. J. Brooks[1] and K. Gillespie-Lynch[1], (1)*The Graduate Center - CUNY*, (2)*College of Staten Island - CUNY*

**Background:**

Although increasing numbers of students with ASD are entering college (Van Bergeijk, et al., 2008), little research focuses on this population. Students with ASD often struggle with the transition to college and from college into the workforce (Adreon & Durocher, 2007; Kapp et al., 2011). The current study utilizes a participatory action approach to develop a peer-mentor intervention for college students with ASD. Peer-mentor interventions may help students with ASD negotiate college life and develop leadership skills (Adreon & Durocher, 2007; Caldwell, 2010).

**Objectives:**

1) Develop a peer-mentor intervention for students with ASD.

2) Evaluate if it meets participants' needs.

3) Examine its applicability to other populations.

**Methods:**

During the spring, participants with ASD (*N*= 12) and other disabilities (*N*= 15) attended weekly hour-long social skills, academic and employment trainings. Social skills trainings were adapted from the PEERS model (Laugeson & Frankel, 2009).

Participants completed assessments (Social Responsiveness Scale [SRS], Spielberger State-Trait Anxiety Scale, Rosenberg Self-Esteem Scale, and a self-advocacy questionnaire) and

participated in focus groups at the end of each term (fall post-tests will be conducted this December). Spring focus group data were coded for "self-advocacy" (students address concerns directly) versus "other-advocacy" (others address their concerns) and the perceived need for social skills training: kappa = 1.0.

During the fall, students with ASD (N=16) and other disabilities (N= 25) participated in hour-long weekly self-advocacy groups and optional one-on-one mentoring sessions. Self-advocacy training focused on self-knowledge, knowledge of rights, communication skills and leadership skills (Test, 2005); training was adapted from a curriculum developed by Valerie Paradiz (a self-advocate). Despite a need for self-advocacy training for autistic individuals (Shore, 2004; Wehmeyer et al., 2010), no published research documents self-advocacy trainings for this population and few self-advocacy interventions include leadership.

**Results:**

Social symptoms $t$ (24) =2.82, $p$ = .01 and anxiety $t$ (24) =2.81, $p$= .009 decreased following spring participation.

Spring focus groups revealed that students often felt social skills training had not been needed (53% of responses). Many statements about advocacy were other-initiated (34%). Thus, we developed a self-advocacy intervention for the fall.

Fall self-advocacy assessments revealed that participants (regardless of diagnosis) had little knowledge of their rights and limited leadership skills. SRS scores were negatively associated with self-esteem $r$ (31) = -.56, p< .001 and self-advocacy skills $r$ (31) = -.76, p< .001. Many students defined self-advocacy as self-esteem.

**Conclusions:**

A participatory action approach revealed that many students with ASD or other disabilities were more interested in self-advocacy trainings than social skills trainings. Many reported having had to practice social skills in "resource rooms" in high school. Students desired help developing self-esteem (which may not be helped by social skills interventions: Wasico et al, 2013) and self-advocacy skills. Many did not know that adults with disabilities are protected by the Americans with Disabilities Act. Few had had opportunities to develop leadership skills. This approach to intervention addresses a key ethical challenge in autism research: ensuring that the research is relevant to people with ASD (Pellicano & Stears, 2011).

**141.112 112** Evaluating the Impact of Emergency Room Services for Children and Adolescents with Autism Spectrum Disorder. M. Milen*[1], D. B. Nicholas[1], L. Zwaigenbaum[2], B. Muskat[3], W. Craig[2], A. (. Newton[2], W. Roberts[4], P. Burnham Riosa[5], R. Sharon[2], A. Greenblatt[3], S. Ratnapalan[6], J. Cohen-Silver[3] and R. Morris[3], (1)*University of Calgary*, (2)*University of Alberta*, (3)*The Hospital for Sick Children*, (4)*University of Toronto*, (5)*York University*, (6)*The Hosptial for Sick Children, University of Toronto*

Background:

Children with Autism Spectrum Disorder (ASD) are in frequent contact with health and mental health services, yet experience difficulties in accessing appropriate care. This study complements an ongoing study examining hospital-based inpatient care for children and adolescents with ASD, focusing specifically on experiences related to care delivery in the emergency department (ED). Negative experiences in the ED have the potential to create or exacerbate deleterious health and mental health consequences for children with ASD, and can create challenges for health care providers (HCPs). Review of these domains will provide a critical lens through which to examine the practices, policies, experiences, and processes that impact children and youth with ASD in the ED The study will identify key issues related to patterns, experiences and processes of ER care for children and youth with ASD, while generating recommendations for practice and policy.

Objectives:

This multisite study looks to (1) identify experiences related to accessibility and navigation of the ED, (2) examine how health care providers experience interactions with children with ASD and their families, and (3) identify gaps and opportunities for improvement in ED services. The ultimate goal is to identify potential strategies to improve ED protocols and care for children and adolescents with ASD.

Methods:

Semi-structured qualitative interviews were conducted at the Stollery Children's Hospital in Edmonton, Alberta, and the Hospital for Sick Children in Toronto, Ontario. To date an n=20 families, and n=14 HCPs have participated in the study across both sites. Using a purposeful sampling approach, the study is recruiting across levels of ED care, and includes: (a) young persons with ASD (to age 18 years) who have recently sought emergency health care at either ER sites; (b) their parent(s); (c) inter-professional ER care providers, (d) community clinicians in Edmonton and Toronto serving children and youth with ASD utilizing ERs, (e) administrators and policy-makers in Edmonton and Toronto who set directions, establish services, and facilitate evaluation of ER services. Continued data collection efforts across sites will ensure sample diversity.

Results:

Emerging themes common to participants and HCPs include: (1) challenges associated with ED waiting times and HCP transparency in care delivery; (2) disclosure of a child's ASD to HCPs and ED staff; (3) the importance of HCPs abilities to effectively and appropriately engage with, and establish baseline in, children and youth with ASD; (4) HCP utilizing parent/caregiver as expert on the child with ASD (e.g., baseline presentation, known behaviours, sensitivities); (5) HCPs utilizing parent/caregiver to maintain stability during treatment (6) continued education for HCPs to ensure best practice standards are met when working with children and youth with ASD (e.g., documentation, video, toolkits).

Conclusions:

This study depicts the ED experiences of children and youth with ASD, their families, and their HCPs. It offers guidance to ED health care providers by proposing practice guidelines and policy recommendations. Proposed practice implications of this research include the creation of toolkits for parents and HCPs, and the development of a more ASD-friendly ED environment for families.

**141.113 113** Evaluation of a 3 Day Autism Training Model in Nigeria.

C. Flint*[1], K. Hench[2] and J. Salt[1], (1)*HAVE Dreams*, (2)*AACTION Autism*

Background:

Throughout Nigeria, there is little Autism awareness and intervention. Individuals with autism are largely undiagnosed or misdiagnosed. This leads to difficulties integrating into communities, receiving appropriate services, and a vulnerability to mistreatment. However, more parents and professionals are becoming familiar with the unique characteristics of Autism Spectrum Disorders.

AACTION Autism, a U.S. based non-profit organization dedicated to worldwide awareness through training, partnered with The Learning Place Centre in Lagos, to provide a 3 day intensive training based on structured teaching principles.

Structured teaching is a specific instructional strategy designed to accommodate the characteristic strengths and neuropsychological differences of those with autism.

During our training, participants learned how to apply interventions across a range of skill sets. The participants observed the trainers work with one child each day (concrete learners, intermediate learners and high functioning learners). The training is multi-modal in that it includes lectures, video demonstration, and opportunities to create structured activities that were then implemented with students for observation by participants.

The U.S. model for the training program has been evaluated and proven to be successful (IMFAR, 2012; BPS 2010). However, the implementation of the training model in Nigeria is unknown, due to more limited resources, potential cultural barriers and different expectations by parents and professionals of individuals with autism.

Objectives:

This study investigated the preliminary effectiveness of the training model to increase parent and professional competence to set up structured teaching programs in Nigeria. The study addressed (i) competence of autism programming gained across each day of the 3 day training and (ii) the satisfaction with the training model.

Methods:

Participating professionals and parents (n= 37) who attended the training completed a structured questionnaire pre and post training on each day.

The questionnaire was developed and piloted by the lead trainers to assess key aspects of structured teaching interventions. The final questionnaires were piloted on several Nigerian residents for ease of readability and cultural sensitivity.

Each questionnaire described a student with skills sets at either the concrete level (early learner); intermediate level; or abstract level (advanced learner). Participants answered questions on each day regarding that child. Each questionnaire had 4 questions, with a maximum total score of 16.

Results:

i) T-test revealed that there was a significant ( $p<.001$) increase in competence scores pre and post training at each level of development (concrete, intermediate, abstract).

ii) Satisfaction with the training model was very high. 100% (n=37) of responders felt more prepared to address the needs of individuals with ASD having attended the training.

Conclusions:

The 3 day autism training program was successfully implemented in the Nigerian capital. By attending the training, participants increased their confidence in their ability to teach the autism curriculum, at any level of ability, to individuals with ASD. Both parents and professionals satisfaction with the training was very high. These results indicate the preliminary effectiveness of our training program. A more rigorous methodology is needed to extend confidence in these evaluation results.

**141.114 114** Examining Change in Motivation to Modify Teacher Behavior Following Training on Evidence-Based Practices for Students with Autism Spectrum Disorder. M. L. Rinaldi*, K. V. Christodulu and L. Corona, *University at Albany, SUNY*

Background: Current research has indicated that using best practices for educating students with autism spectrum disorder (ASD) in the classroom can produce positive successful outcomes (Iovannone et al., 2003). Despite the documented success of evidence-based educational practices for students with ASD, translation of research to real-world application in school settings is often lacking (Burns & Ysseldyke, 2009; Hess, Morrier, Heflin, Ivey, 2008) and little is known about why the research-to-practice gap exists (Callahan, Henson, & Cowan, 2008). One potential area of investigation is examining teachers' motivation to use evidence-based practices for students with ASD.

Objectives: To examine teachers' motivation to change the practices used for students with ASD prior to and following a series of trainings on evidence-based practices for students with ASD.

Methods: A modified version of the University of Rhode Island Change Assessment (URICA; E. A. McConnaughy, J. O. Prochaska. & W. F. Velicer, 1983) was given to teachers across New York State from 2011-2014 to assess the teachers' "stage of change" prior to and following a series of training on best practices for educating students with ASD. Training was conducted by the Center for Autism and Related Disabilities at the University of Albany (CARD Albany) and consisted of five full-day sessions over a three-month period that employed a research-based capacity building model. A cluster analysis was performed on the pre- and post- training data to examine the number of motivational subtypes in each sample and the percent of individuals in each subtype.

Results: Preliminary results of the study (data collection ongoing) support the existence of two subtypes – ambivalent and participation. Initial results suggest that prior to training, 64.7% of teachers fell in the ambivalent cluster (reluctant about changing their behaviors) and 35.3% of teachers fell in the participation cluster (invested and involved in behavior change). Following training, preliminary data indicates 73.5% of teachers were in the participation cluster while 26.5% of teachers were in the ambivalent cluster. Overall results indicate a greater number of teachers were in a higher readiness stage following training.

Conclusions: The stages of change model has been used successfully to assist in the tailoring of treatments related to health behaviors and psychotherapy change (Norcross, Krebs, & Prochaska). Knowledge about changes in teacher motivation to modify teaching practices for students with ASD following training in evidence-

based practice can provide important information that could assist in future instruction of educators.

**141.115 115** Families of People with Autism on Curaçao Need Support. R. Pin*[1] and E. M. Blijd-Hoogewys[2], (1)*University of the Netherlands Antilles*, (2)*INTER-PSY*

Background:

On Curaçao, a Small Island Developing State, support systems for people with autism are still developing. Over the years, a lot has been done by local healthcare facilities. Several local psychiatrists, speech therapists, psychologists, and other professionals dealing with autism became more experienced and knowledgeable about the support needed. Also schools, especially special education, have taken steps to facilitate children with autism.

Despite the apparent improvement in care and support, there are indications that (families of) people with autism still lack support. Therefore, this study looks at a wide range of issues, with a focus on problems experienced in the diagnostic process, treatment, housing, education, work and leisure, socializing and wellbeing.

Objectives:

The objective of this study was to gain insight in the need for professional support in people with autism living on Curaçao and their families, to identify the gap between this need for support and the availability of resources and facilities. The local parents' association 'Asosiashon pa Autismo Curaçao' (AAC) will use the results of this study to bring the needs experienced to the attention of social organizations and the government.

Methods:

Using a mixed method approach, first a focus group (qualitative research) was held consulting 7 parents from the AAC concerning their needs for support for their children with autism. Next, these results were used as a local input for the construction of a questionnaire (quantitative research) based on the Dutch Society of Autism 2013 questionnaire. 32 parents and caregivers of children with autism (29 mothers, 1 father, 1 teacher and 1 therapist) filled out the survey online or hardcopy in the Dutch or Papiamentu language.

Results:

The study reveals that the diagnostic process takes long and in many cases parents still need to go abroad to get a correct diagnosis. Parents express the need for a multidisciplinary team and for case managers. After diagnoses, parents experience that there is no care or treatment plan and no guidance to the right facilities. Only a few schools have autism experience; in some cases children are rejected at all schools and are not able to receive any education. Parents perceive housing facilities to be scares; although in the small community family provides a strong safety net, there is a strong need for assisted living, as parents fear for the time that they will no longer be around. The respondents are aware of leisure facilities on the island, but they refer to the broader range of possibilities in e.g. Venezuela and the Netherlands. A job coach could improve job opportunities. Many parents experience financial difficulties. Furthermore, parents perceive there is still a taboo on autism in the Curaçao community; they fear that a lot of children stay undiagnosed and might end up on the wrong pathway. They see a role for the government.

Conclusions:

To improve the professional support on Curaçao for (families of) people with autism, institutions should collaborate to facilitate the route from first diagnosis to integrated support for care, education, living, work and wellbeing.

**141.116 116** Follow-up Study of Education Graduates Reveals Sustained Use of Evidence-Based Practices. L. J. Hall* and S. McDaniel, *San Diego State University*

Background:

Training and sustaining the use of evidence-based strategies by special educators of students on the autism spectrum is a priority for the field because using effective practices with fidelity is related to better outcomes (Durlak & DuPre, 2008). Unfortunately, many special educators who are trained do not stay in the field and the turn over rate is increasing (McLeskey & Billingsley, 2008). Even if they do remain in the field, special educators report using strategies supported by research with equal frequency to those that are not evidence-based (Burns & Ysseldyke, 2009) and survey results of educators working with children with autism spectrum disorders (ASD) reveal that effective teaching practices are

implemented at low levels (Hendricks, 2011; Hess, Morrier, Heflin & Ivey, 2008).

Objectives:

This poster will contain the results of a follow up study of the San Diego State University's Masters degree program with a specialization in Autism. SDSU also has a mentor program where graduates received training in coaching and effective supervision and serve as mentors for current candidates. Multiple measures were used to determine the following research questions: Do graduates 1) remain in the field and 2) sustain their use of evidence-based practices (National Standards Project, 2009; Odom, Collet-Klingenberg, Rogers & Hatton, 2010).

Methods:

Multiple measures that were used in this study included: a Qualtics survey sent to program graduates that included questions about current positions and use of evidence-based practices and progress monitoring systems as well as indication of factors that sustain practices. Video samples from a subset of graduates were used to score the fidelity of implementation of evidence-based practices by 2 inter-raters using the checklists from the NPDC on ASD. Interviews were conducted with a subset of graduates to obtain information about the program factors that facilitated the sustained use of evidence-based practices.

Results:

Results of a survey sent to 65 graduates reveal that 94% remain in the field 1 to 7 years following graduation and that they report using the 24 evidence-based practices identified by the NPDC on ASD often or very often. Video samples of the educators implementing select evidence-based practices obtained from 19 graduates were scored as being used with fidelity for a mean of 89% (range 78 – 100%) of strategy components. 98% of graduates report that they continue to collect data for student progress monitoring purposes. 100% reported that the program contributed to their capacity to use evidence-based practices and sustain these practices over time. The main program components that graduates stated effected sustained practices included: Support from peers in the cohort; knowledge about research based strategies used with individuals with ASD; opportunity to participate in field experiences & conferences; and opportunity to practice skills with a coach during practicum.

Conclusions:

The SDSU Masters Degree/Autism specialization program with an embedded BACB approved course sequence and a mentor program for graduates resulted in the creation of a strong community of practice that supported graduates who sustained their use of evidence-based practices and ongoing progress monitoring when educating learners with ASD.

**141.117 117** From Research Settings to Parents: The Referral Sources of Evidence-Based and Non Evidence-Based Practices. K. Pickard* and B. Ingersoll, *Michigan State University*

Background: Literature in the ASD field has repeatedly highlighted the need for a more effective framework of disseminating evidence-based practices into community settings. Despite a significant amount of research that has documented the types of services that are being used by parents of children with ASD, research has yet to determine who recommends parents to specific intervention practices and, more generally, how intervention-related knowledge spreads to parents. As a result, the current study seeks to clarify the process by which interventions are disseminated to parents. Research has noted that health recommendations can come from both formal (i.e. individuals who are paid for the services they provide) and informal (i.e. unpaid individuals such as family and friends) individuals. As in other health fields, parents of children with ASD make critical decisions about services and treatments for their child based off of advice that they seek out from other individuals.

Objectives: The current study sought to examine 1.) the types of services primary caregivers are accessing for their child with ASD, and 2.) the specific professionals and individuals who are the referral sources of evidence-based and non evidence-based practices.

Methods: 244 primary caregivers of a child with an ASD diagnosis between the ages of 2 and 17 ($M$=6.17 years) completed an online survey that assessed the following: basic demographic information, ASD symptom severity, social

network size, social network makeup, social network density, autism services accessed, parenting stress level, and social support. Service recommendations were broken down in order to analyze which specific professions and individuals were making recommendations to both evidence-based and non evidence-based practices.

Results: Primary caregiver service is depicted in Figure 1. 94.67 % of primary caregivers were accessing at least one evidence-based practice for their child and 58.20% were accessing at least one non-evidence-based practice for their child. A Pearson's chi-square was run in order to determine whether social network formality (i.e. formal or informal individuals) significantly predicted whether a recommendation was made to an EBP (i.e EBP or non-EBP). The chi-square was significant [$X^2(6)=253.96$, $p<0.001$], indicating that formal social network ties were significantly more likely to make recommendations to an EBP. Moreover, an odds ratio indicated that formal recommendations were 10.17 times more likely to make a recommendation to an EBP. Specific recommendations within each profession are provided in Figure 2.

Conclusions: Research within the ASD field has already documented the importance of individual recommendations in the choices that parents make about service use for their child with ASD. The present study clarifies the nature of these recommendations. Given the significant research to practice gap within the ASD field, the current study provides important implications for the ways in which we disseminate EBPs to parents.

**141.118 118** Happy Wives and Happy Husbands: Actor-Partner Associations Among Mothers and Fathers of Children with Autism. N. Ekas*, L. Keylon and M. Pruitt, *Texas Christian University*

Background: Raising a child with an autism spectrum disorder (ASD) is a stressful experience for parents and results in lower well-being (Ekas et al., 2009). The stress that parents face can manifest in ways that affect them individually and as a couple. Studies have found that relationship satisfaction is an important factor in understanding parents' experiences and is impacted differently for mothers and fathers (Hartley et al., 2011). Since relationship satisfaction is an important predictor of parental adjustment it is important to examine factors that enhance satisfaction. One potential factor is benefit finding, which has mixed effects on positive outcomes (Samios et al., 2011). Parent depression may also impact the quality of parents' relationships (Kouros et al., 2011).

Objectives: The purpose of the present study was to further understand the factors that influence relationship satisfaction in couples raising a child with ASD by examining the effects of both depression and benefit finding. The current study also examines these factors not in isolation to the impact on the individual but also on the impact on the other partner's relationship satisfaction.

Methods: Seventy-two heterosexual couples participated in the current study (94% married). Parents were predominantly Caucasian or Hispanic. The average age of fathers was 38.25 years while the average age of mothers was 42.63 years. All parents reported their child had a diagnosis of an ASD. Parents completed questionnaires assessing marital satisfaction (Couples Satisfaction Index), depression (Center for Epidemiological Studies - Depression), and benefit finding (Benefit Finding Scale).

Results: Because the data consisted of individuals nested within dyads (i.e., mother and father) we used Hierarchical Linear Modeling. The Actor-Partner Interdependence Model (APIM; Kenny et al., 2006) was used to examine the effect that an individual's independent variable has on their own dependent variable (actor effect) as well as his/her partner's dependent variable (actor effect). Two separate APIM models were tested to examine the effects of benefit finding and depression on relationship satisfaction. Results indicated that an individual's benefit finding was positively associated with their relationship satisfaction ($b$ = .92, $SE$ = .19, $p$ < .001) as well as their partner's relationship satisfaction ($b$ = .56, $SE$ = .19, $p$ < .01). An individual's depression negatively predicted their relationship satisfaction ($b$ = -1.23, $SE$ = .32, $p$ < .001) and their partner's relationship satisfaction ($b$ = -.61, $SE$ = .32, $p$ = .06).

Conclusions: Previous research has found relationship satisfaction to be adversely affected in families of children with an ASD. Given the dyadic nature of relationships, we focused on how mothers and fathers impacted each other. Our results indicated that being able to find benefit in

their child's disability was associated with higher levels of relationship satisfaction for themselves and their partner. On the other hand, depression negatively impacted relationship satisfaction of the individual and their partner. The findings of this study have important clinical implications with respect to understanding the dyadic nature of relationship satisfaction and how we might improve levels of relationship satisfaction among families experiencing high levels of stress.

**141.119 119** Health Care Transition Services for Youth with Autism Spectrum Disorders. K. A. Kuhlthau*[1], M. Erickson Warfield[2], J. Delahaye[1], A. Shui[3], M. K. Crossman[2] and E. Van Der Weerd[4], (1)*Massachusetts General Hospital*, (2)*Brandeis University*, (3)*Massachusettes General Hospital for Children*, (4)*Harvard University/Massachusetts General Hospital*

Background:

Pediatric societies and the Maternal and Child Health Bureau endorse the notion of transitioning to adult services. The National Survey of Children with Special Health Care Needs showed that only 21% of youth with ASD received a set of transition planning services whereas for other youth with special needs 42% received transition planning services (Cheak-Zamora et al 2013).

Objectives:

We sought to describe the health are transition services youth with ASD received, satisfaction with those services, the services families desired, and barriers to receiving care. We further describe the covariates of receipt of services.

Methods:

This is a cross cross-sectional survey or parents of youth (age13-26) with ASD living in the community. We examined descriptive data on receipt of transition services, desire for the services, and barriers to use. We further examined demographic and health-related characteristics associated with receipt of services.

Results:

This is a relatively well off group of families. Receipt of transition services was low overall. It ranged from 3% of the sample receiving a written transition plan, to between 10 and 20% of respondents who indicated that youth received informative materials about the transition process (17%), help with teaching the child to manage their own health care needs (19%) and other transition-related services or support (13%). Even fewer respondents reported getting information on adult medical specialists (11.8%) and support in searching for an adult PCP (7.3%). Similarly low percentages of respondents reported getting a written medical summary (9%) or getting information about guardianship (9%). Overall, only 60% received any transition service. Reciept of these services was related to symptoms of anxiety and depression. In general, satisfaction for the services that were received was quite high with nearly everyone reporting that they were somewhat or fully satisfied. The low levels of use are in sharp contrast to the high percentage of parents who would like the services that they don't currently receive. Between 65 and 90% of families wanted each of these HCT services.

Conclusions:

Our findings suggest that there is a great need to address the provision of HCT services for youth with ASD. Families who have the services are generally satisfied and those who do not have them generally want them. We further found that parents reported barriers to obtaining these services at high levels with a particular desire for more information and adult providers who could better meet their needs

**141.120 120** It's Time to Clean up! Symptom Severity Impacts Compliance Behaviors in Children at-Risk for Autism. N. Ekas*[1], N. M. McDonald[2] and D. S. Messinger[3], (1)*Texas Christian University*, (2)*Child Study Center, Yale University*, (3)*University of Miami*

Background: One of the important developmental milestones during the toddler years is the ability to comply with others' requests (Kopp, 1982). During tasks that require compliance (e.g., clean-up tasks) toddlers may demonstrate committed compliance (i.e., willingly embracing the rules) or situational compliance (i.e., obeying the rules but only after repeated reminders). On the other hand, toddlers may also display noncompliant behaviors that include defiance, resistance, or passively ignoring requests to follow the rules. Child noncompliance has been shown to be associated with later behavior problems whereas compliance is associated with adaptive social behaviors (Kuczynski & Kochanska, 1990). Children with autism spectrum disorder (ASD) have been found to exhibit heightened levels of behavior problems

and maladaptive social behaviors and are more noncompliant than their typically developing peers (Bryce & Jahromi, in press). The younger siblings of children with autism often show subclinical deficits that may include behavior problems.

Objectives: The purpose of the current study was to examine the association between autism symptom severity and later child compliance in a group of toddlers at-risk for an autism spectrum disorder.

Methods: The sample consisted of 52 children who were the younger siblings of a child with an ASD (male *n* = 46, female *n* = 30) and 33 children with no family history of autism. Children completed the Autism Diagnostic Observation Schedule at 30 and 36 months of age and a calibrated severity score was calculated. At 36 months, children participated in a clean-up task where the parent was instructed to have their child clean-up like they normally would at home. This task lasted five minutes or until all of the toys were placed in the basket. Child compliance was rated every 15-s and scores reflecting the proportion of time engaged in compliance (committed and situational) and noncompliance (passive, resistance, and defiance) were calculated.

Results: Children at-risk for an ASD were significantly less likely to engage in committed compliance, $F(1,83)=4.67$, $p < .05$. Among the group of children at-risk for an ASD, at 36 months, we found that higher levels of symptom severity predicted lower levels of committed compliance, $b = -.09$ ($SE = .04$) and higher levels of situational compliance, $b = .07$ ($SE = .03$). In addition, those children who received an eventual diagnosis of an ASD were more likely to engage in passive noncompliance, $F(1,47)=5.54$, $p < .05$. We are currently coding parent behaviors during the clean-up task and intend to examine those behaviors in relation to child behaviors during the same task.

Conclusions: The results of the current study support previous work suggesting lower levels of compliant behavior among children with an ASD (Bryce & Kahromi, in press). This study, however, is the first to examine these among children who are at-risk for an ASD. The results have important implications for our understanding of the development of autism, as well as clinical implications for interventions targeting at-risk children.

**141.121 121** Knowledge of Autism for Parents with Low Literacy: Description and Relationship to CHILD Development Knowledge.

J. Campbell*[1], Z. Stoneman[2], D. Greenberg[3], P. Gallagher[3] and C. A. Simmons[4], (1)*University of Kentucky*, (2)*Institute of Human Development and Disability, University of Georgia*, (3)*Georgia State University*, (4)*University of Georgia*

Background: Parents are often the first to note delays in child development and concerns indicative of an autism spectrum disorder (ASD). "Learn the Signs. Act Early" (LTSAE) is a public health campaign targeting improved awareness of early developmental delays and symptoms of ASD. Concerns have been raised regarding the utility of LTSAE materials for various groups, such as parents with low literacy; efforts to modify materials to better inform parents with low literacy are needed to maximize their impact. To tailor public health messages, it is critical to understand what parents with low literacy know about ASD.

Objectives: Investigators documented participants' knowledge about autism and determined areas of limited knowledge. Investigators examined relationships between participants' general knowledge of child development and autism knowledge. The overall goal of the research was to identify content for future LTSAE campaigns and explore relationships between autism knowledge and knowledge of general child development.

Methods: Forty-one participants (32 mothers, 9 fathers; *M* age = 25.03; *SD* = 6.41 yrs; 92.7% African-American) with low literacy (*M* grade-equivalent for reading = 5.83; *SD* = 1.46) completed interviews to assess their (a) knowledge of autism, (b) knowledge of developmental milestones featured in LTSAE materials, and (c) knowledge of other motor, language, social, play, and cognitive developmental milestones. Autism knowledge was assessed via the 22-item Knowledge of Autism (KOA) scale, knowledge of LTSAE milestones was assessed via a 14-item LTSAE Survey (LTSAE-S), and knowledge of additional developmental milestones was assessed via a 16-item survey of development (OTHER). Participants could respond to the KOA items with a "Don't Know" response. Readability of surveys

fell within the 4th-5th grade reading level; scores were calculated by adding number of items correctly answered. For the KOA, "Don't Know" responses were calculated separately.

Results: KOA scores ranged from 0-18 (*M* = 8.15; *SD* = 7.13). KOA "Don't Know" responses ranged from 0-22 (*M* = 10.89; *SD* = 9.47). LTASE-S scores ranged from 2-14 (*M* = 8.05; *SD* = 3.11); OTHER scores ranged from 3-11 (*M* = 7.61; *SD* = 1.69. The KOA item asking if autism affected races equally was correctly endorsed by a high of 56% of participants; the KOA item asking if autism affected boys and girls at the same rate was correctly endorsed by a low of 7% of participants. Several indicators of autism were correctly identified by fewer than 25% of participants: difficulty with eye contact, problems with pretend play, and focusing on single topics. KOA scores did not correlate with LTSAE-S scores, *r*(39) = .27, *ns*, or OTHER scores, *r*(39) = .27, *ns*. "Don't Know" scores also did not relate to LTSAE-S or OTHER.

Conclusions: Parents with low literacy reported variable knowledge about autism, including indicators of autism, such as poor eye contact and pretend play skills. Knowledge of autism did not correlate with knowledge of other developmental milestones, suggesting that parent knowledge of general milestones may not equal knowledge about problems suggestive of autism. Findings highlight the need for specific information about ASD for parents.

**141.123 123** Prevalence and Predictors of Complementary and Alternative Medicine Use Among Children with Autism Spectrum Disorders. A. A. Owen-Smith*[1], S. Bent[2], F. L. Lynch[3], K. J. Coleman[4], V. M. Yau[5], K. A. Pearson[3], M. L. Massolo[5], M. E. Pomichowski[4] and L. A. Croen[5], (1)*Kaiser Permanente Georgia*, (2)*University of California San Francisco*, (3)*Kaiser Permanente Northwest*, (4)*Kaiser Permanente Southern California*, (5)*Kaiser Permanente Northern California*

Background: Approximately 1 in 88 children in the U.S. is diagnosed with Autism Spectrum Disorder (ASD). Unfortunately, there is no identified etiology or definitive cure for ASD. Therefore, it is not surprising that many parents turn to complementary and alternative medicine (CAM) therapies for their affected children. Prior studies have suggested that CAM use is common in this population; however, these studies have been limited by small samples and an inability to assess response rates.

Objectives: The purpose of this analysis is to examine the prevalence and predictors of CAM use among a group of geographically and racially/ethnically diverse children with ASD who are enrolled in the Mental Health Research Network (MHRN) Autism Registry, a database of children diagnosed with ASD who are members of one of the 10 public-domain health systems affiliated with large integrated health care systems within the HMO Research Network.

Methods: A Web-based survey of parents of children with ASD was implemented at four MHRN Autism Registry sites in order to obtain information not available in health plan databases including parents' use of CAM with their children who have ASD. Parents were asked to report what CAM therapies they have ever used or used within the past three months to treat their child with ASD, what they have paid for these therapies and the degree to which they perceived them to be harmful or helpful. The domains of CAM therapies on the survey included products (e.g., vitamins), practices (e.g., acupuncture) and providers (e.g., chiropractic). Quality of life, caregiver strain and other sociodemographic and clinical characteristics were also assessed.

Results: A total of 1,063 survey respondents answered the CAM-related questions; of these, 919 (~86%) reported ever using CAM to treat their affected child. The most common CAM providers used were chiropractors (20%); the most common CAM practices used included massage (71%) and meditation (19%); the most common CAM products used included multivitamins (89%), fish oil (38%) and melatonin (34%). Respondents spent an average of $1,164.26 on CAM providers and an average of $112.41 on CAM products in the past 3 months. Massage, chiropractic, acupressure and melatonin were perceived to be the most effective CAM modalities. Parents who were separated/divorced and had older children were significantly less likely to report recent CAM use while parents of children who had used prescription drugs in the past three months were significantly more likely to report recent CAM use. Quality of life and caregiver strain were not associated with CAM use in this population.

Conclusions: CAM use is common among children with ASD. Knowledge of specific CAM therapies that are most commonly used and predictors of CAM use may assist clinicians in counseling families and promoting safe use. Parental perceptions of effective therapies may help guide in the selection of specific CAM therapies for future studies.

**141.124 124** Prevalence of Multi-Sector Treatment for Young Children with Autism Spectrum Disorder. L. A. Bilaver*[1], L. Cushing[2] and A. Cutler[2], (1)*Northern Illinois University*, (2)*University of Illinois Chicago*

Background:

The period of early childhood (ages 3-5 years) often marks the shift from a focus on early intervention and diagnosis of autism spectrum disorder (ASD) to a focus on treatment. Preschool aged children with ASD and their families often experience changes in treatment that mark the transition from early intervention to preschool special education services. In addition, families may be establishing treatment plans that include school-based and clinic-based services. Despite the significance of this period for the treatment of ASD, little is known about the prevalence of treatment overall or within specific sectors.

Objectives: To estimate the prevalence of treatment for ASD among a nationally representative sample of preschool aged children with autism enrolled in preschool special education services. Rates of treatments both inside and outside of school are estimated and correlates of treatment are identified.

Methods:

Data from the Pre-Elementary Education Longitudinal Study (PEELS) are used to identify the study population of children with parent or teacher identified autism. The PEELS is a nationally representative sample of 3,104 children ages 3-5 receiving special education services during the 2003-04 school year. A subsample of 246 children with ASD is used in the analysis. Bivariate and multivariate methods are used to analyze the complex survey data. Generalized estimating equations are used to estimate the population average effect of child, family, and school district characteristics on the likelihood of receiving treatment including speech, occupational, or physical therapy, behavior therapy (including applied behavior analysis), and mental health services.

Results:

14.3% of children with ASD received one of five treatment services both at school and outside of school at wave 1. The percent decreased to 11.5% three years later. Speech and occupational therapy were the two most common treatments across time with 90.5% and 65.4% of children receiving these services respectively at wave 1. Speech therapy was the service most often received both inside and outside school (12.4% wave1, 10.4%, wave 2, and 13.9% wave 3). Behavior therapies were received by 4.7% of children in wave 1 and 6.9% in wave 3. Significant decreases in the percent of children receiving speech therapy over time were detected even after controlling for severity of disability ($p<.0.05$). Beyond severity of disability, we could not detected significant correlates of receiving services overall in multivariate analyses; however, the adjusted odds ratio (OR) of receiving occupational therapy both inside and outside school was greater for children with higher family incomes (OR 3.16, 95% CI: 1.37-7.29) while children whose mother's had a high school diploma or less had lower odds of receiving speech therapy in both settings (OR: 0.28, 95% CI: 0.11-0.70)

Conclusions:

The results reveal that a small percent of children with ASD receive treatment services in multiple settings. Overall rates of treatment decline during the preschool and early elementary school years. Socioeconomic disparities in treatment are evident in multi-sector use of speech and occupational therapies. The low rates of some treatment services and particularly multi-sector treatment raise questions about access to treatment and treatment planning.

**141.125 125** Profile and Predictors of Service Needs in ASD. S. Hodgetts*[1], L. Zwaigenbaum[1] and D. B. Nicholas[2], (1)*University of Alberta*, (2)*University of Calgary*

Background: The rising prevalence of autism spectrum disorders (ASD) is straining health, education and community service systems. Tailoring supports and services to best meet families' needs could improve families' quality of life and decrease burden on these systems over

time, yet little is known about service needs from the perspective of families.

Objectives: This study evaluated service needs from the perspective of families. Specific objectives were to identify:

1. Families' most frequently identified overall service needs;
2. Families' most frequently identified unmet service needs;
3. Families' best met service needs;
4. Child and/or family variables that predicted overall needs and unmet service needs.

Methods: 143 parents of a child with ASD (mean age = 9.8 years) completed a survey including demographic and descriptive information, an adapted version of the Family Needs Survey–Revised (FNS-R), and an open-ended question about their "single greatest service need". Descriptive statistics were calculated to characterize the sample, and determine the degree to which items were identified as needs and those needs were met. Simultaneous multiple linear regression analyses were used to determine predictors of total and unmet needs. Qualitative responses were content analyzed.

Results: Based on the FNS-R, the most frequently identified overall needs were for information on current (82%) and future (79%) services, handling disruptive behaviors (77%), and support to find personal time (74%). The greatest unmet needs were for information on services available currently (39% unmet) and in the future (61% unmet), support to find personal time (43% unmet), and locating respite care (39% unmet). Most participants reported positive experiences with the funding available for services (73-85% needs met across items) and quality of professional support (68-94% needs met across items). The most frequently identified "single greatest service needs" were respite care (26%), planning for and availability of adult services (20%) and transparent information about services (19%). Decreased child's age and household income, disruptive behaviors, and increased maternal age predicted more total needs and unmet needs.

Conclusions: Information on services, handling disruptive behaviors, and parent and child respite support were key needs. However, these most frequently identified overall needs were often the greatest unmet needs. Age, disruptive behavior and income, but not language and intellectual abilities, predicted overall and unmet needs. Our discussion will include potential reasons for the identified predictors, and suggestions for how to target practices and policies to best meet families' needs in the context of current resources.

**141.126 126** Quality of Life of Families with a Child with ASD on an Applied Behaviour Analysis Service Waitlist. M. Lloyd*, S. Jones and E. Bremer, *University of Ontario Institute of Technology*

Background: Family Quality of Life (FQOL) encompasses the physical health, psychological well-being, and social relationships of the entire family. Families of children with ASD often experience extremely long wait-times for disability related services, social isolation, and stress related to the often difficult behaviour of the child with ASD; and this can negatively affect quality of life for these families. It is important to fully understand these challenges to understand how to best support families of children with ASD.

Objectives: The purpose of this study was to investigate the quality of life of families with a child 0-18 years with ASD currently waiting for government funded Applied Behaviour Analysis (ABA) services in the Durham Region of Ontario, Canada.

Methods: All families with a child 0-18 years with ASD on the Durham ABA waitlist (n= 484), were mailed a survey that consisted of six sections of the Family Quality of Life Survey: Main caregivers of people with intellectual or developmental disabilities. Specifically: about your family, health of the family, support from disability related services, leisure and recreation, community interaction, and overall family quality of life were included. In addition to the FQOL questions, parents were asked to report basic demographic information about their child and their child's diagnosis. A self-addressed stamped envelope was included in the envelope along with a cover letter with instructions.

Results: Five surveys were returned to sender, and 151 surveys were returned completed (32% response rate).The average age of the children in

this sample was 7.3 years (19% female) and the average age at diagnosis was 5 years of age. Parents also reported that they had been on the ABA waitlist for an average of 8.6 months and 75% live in a small city or small town. 50% reported that the mother was the primary caregiver for the child with ASD and a further 24% indicated that both the mother and father were the primary caregivers and 81% reported two-parent homes. Only 60% of respondents were satisfied or very satisfied with the health of their family, with 71% reporting physical and/or mental health concerns for their family. 64% indicated that there were disability-related services that their child needed that they were not currently accessing. When asked how important to their family's quality of life the disability-related support services for their child with ASD were, 92% reported that the services were very important or quite important.

Conclusions: Positive developmental outcomes for children with ASD are the result of numerous factors including the overall quality of life of the family. These results indicate that parents feel that access to disability-related services for their child with ASD is very important for their FQOL; however, many families are not accessing these essential services. These results also demonstrate that family members of children with ASD may incur high levels of physical and/or mental health concerns. Future research and programming should target program accessibility and overall family health in order to better serve families of children with ASD.

**141.127 127** Relationships Between Ethnicity and Age of Initial ASD Diagnosis in a Clinical Sample. F. van der Fluit*[1], D. J. Kriz[1], K. E. Zuckerman[2] and A. Landry[3], (1)*Oregon Health and Science University*, (2)*Oregon Health & Science University*, (3)*Pacific University*

Background: Health care disparities disproportionately impact racial and ethnic minorities (Flores et al., 2008; Lasser et al., 2006; Mensah et al., 2005). Factors such as access to care, provider biases, and poor communication and health literacy have been identified as potential explanations for these differences (US DHHS, 2008). These factors, as well as others (Mandell et al., 2005, 2009), have also been implicated as potential reasons for differences in age of diagnosis in ASDs. Although previous research has indicated that there is no difference in the rates of ASDs in different racial and ethnic backgrounds (Bertrand et al., 2001; Croen et al., 2002), there are reported differences regarding the age at which diagnosis occurs (Mandell et al., 2002).

Objectives: The current study will examine age of diagnosis and related demographic and behavioral variables in a group of children referred for diagnostic evaluation.

Methods: 2170 children (1725 males, 445 females) between the ages of 2 and 14 (mean age = 71.81 months, SD = 36.70 months) underwent a comprehensive diagnostic evaluation. The sample was categorized based on caregiver-identified racial/ethnic background: 73.6% (1598) were Caucasian, while 26.4% (572) were from racial or ethnic minority backgrounds (African American, Hispanic, Asian/Pacific Islander, or "Other"). Of the total sample, 829 children (659 males, 170 females; mean age = 62.02 months, SD = 34.61 months) were eventually diagnosed with an ASD; 71.2% (590) were Caucasian and 28.8% (239) were considered racial or ethnic minorities.

Results: In the group as a whole, the mean age at evaluation for the Caucasian group was 72.85 months (SD = 37.01 months); the mean age at evaluation for the Minority group was 68.91 (SD = 35.67 months; $t(2168) = 2.21$, $p = .027$). The groups did not differ in terms of caregiver-reported problem behaviors (CBCL internalizing problems: $t(2077) = -1.12$, $p > .05$; externalizing problems: $t(2077) = 1.71$, $p > .05$; total problems: $t(2077) = 0.50$, $p > .05$). Within the ASD group, the mean age at evaluation for the Caucasian group was 63.95 months (SD = 36.21 months); the mean age at time of evaluation for the Minority group was 57.26 months (SD = 29.86 months; $t(827) = 2.53$, $p = .01$). Caregivers reported that children in the Minority group were exhibiting more internalizing behavior problems ($t(788) = -3.07$, $p = .002$) and more total problems ($t(788) = -2.08$, $p = .038$) than children in the Caucasian group.

Conclusions: These results indicate that in our sample there is a difference in average age at time of evaluation depending on minority status. However, the pattern is not consistent with previous findings suggesting that children from a racial/ethnic minority background are diagnosed at later ages than Caucasian children. Additional

factors, such as developmental level, more specific demographic information, severity of impairment, and caregiver reported behavioral profiles will be further explored in order to better understanding the patterns of similarities and differences between children in these two groups. Clinical implications, future directions, and potential limitations, including referral source, will also be discussed.

**141.128 128** South Carolina Autism Treatment Network: Bridging the Communication Gap Between Community Pediatricians and School-Based Clinicians to Increase Service Coordination. A. V. Hall*[1], R. K. Abramson[1] and H. H. Wright[2], (1)*University of South Carolina, School of Medicine*, (2)*University of South Carolina*

Background: In SC, and many states, a two-tiered system for diagnosis and treatment of individuals with an Autism Spectrum Disorders(ASD) exists. First are the community providers offering early intervention services.Second are the local school systems that provide services to ensure that students of all ages achieve the highest level of learning potential. In the best circumstances, the school collaborates with community providers to provide the best long-term outcome for children with ASD and enhance scarce resources. In reality many children in SC only access services through their pediatrician or the local school districts. Most children with ASD are diagnosed and served by school resources alone; only three percent of children with ASD are diagnosed solely by non-school resources. Of the three percent diagnosed in the community, about half (57%) are served by a combination of school and non-school resources.The other 40% are served by school resources alone (Yeargin-Allsopp et al., 2003). Thus the SCATN believed bridging the communication gap between the two major stakeholders in the diagnosis and treatment of ASD was critical.

Objectives: To create a consensus paper by SCATN pediatricians and school personnel as a road map for best approaches to screening, referral, diagnosis, education services, and treatment of children with ASD to improve student-outcomes in SC.

Methods: Two meetings were held in SC to both provide ASD education and to develop a consensus among health care providers, educators, and child advocates regarding assessment and treatment of children with ASD. Communication continued between meetings and via email and Google documents. At the second meeting, this process produced a consensus paper that was discussed, approved, and disseminated.

Results: The consensus paper provides a roadmap to increase communication between pediatric offices, parents, and local school districts. Many SCATN pediatricians did not understand the process of communicating with a school. The following consensus was reached between school personnel and community health care providers representing part of the roadmap: 1) School Psychologists are the personnel best equipped to communicate with pediatricians; 2) Pediatricians understand that a medical diagnosis of ASD will not always lead to a school diagnosis of ASD or necessitate school based intervention; and 3) All communications should be brief and only relevant information should be exchanged. Important to the consensus process was the educational component. Survey results indicated participants increased their knowledge about ASD and its treatment, with the greatest gains made by pediatricians in the areas of behavioral therapies, community resources, and use of technology, hopefully increasing the likelihood of appropriate referrals and coordination of interventions among school personnel, physicians, and parents.

Conclusions: Crucial to improving the outcome of students with ASD is community collaboration in care, particularly collaboration of pediatric practices with the educational system. Such collaboration addresses other barriers to good care, such as pressures from parents and schools to prescribe medications, cultural biases that may prevent schools from assessing children for ASD or may prevent families from seeking health care, and inconsistencies in recognition and referral among schools in the same system.

**141.129 129** Supported Screening to Enhance Identification of ASDs in Latino Children. B. J. Anthony*, K. Linas, M. Biel, D. Jacobstein, R. Mendez and S. Dos-Santos Arquinio, *Georgetown University*

Background: Screening in primary care is a key step in identifying young children with ASDs in order to expedite early behavioral and educational interventions. However, despite evidence that formal screening improves accuracy of identification over informal clinical assessment,

the use of these tools in primary care is low. Moreover, there is strong evidence of disparities in rates of identification and service utilization for Latino children as compared to non-Latino white children. Here, we present evidence for the effectiveness of an 18-month trial of *Supported Screening (SS)*—developed through a community participatory process including formative research with families and primary care providers (PCPs) and staff--to enhance the uptake of universal screening for ASDs in a large primary care center serving a primarily Latino population and increase identification of children with ASDs.

Objectives: The goals of *SS* are to enhance the identification of ASDs and other developmental delays in Latino children by increasing: (1) screenings conducted at 18- and 24-month well-child visits; (2) positive screens; and (3) successful referrals and timely evaluations.

Methods: *SS* has been implemented at the Upper Cardozo site of Unity Health Care (UC-UHC) in the District of Columbia and includes three components: (1) formative research and outreach activities*;* (2) 5-session training for primary care providers (PCPs), and (3) Family Navigators (FN) with lived experience who provide support to families (in person and phone contact) with a child identified at risk for ASD as well as ongoing care coordination with early intervention and medical providers. Screens and referrals are tracked for the approximately 6000 0-36 month old children per year who receive care at UC-UHC (80% are identified as Latino).

Results: Formative research with PCPs and families, including cognitive interviewing, resulted in adaptation of M-CHAT administration (oral format, shared screener implementation by family navigators and PCPs) and a focus on engaging families/addressing barriers in PCP training, coupled with ongoing consultation. Evaluations showed significant increases in PCP knowledge of autism, evidence based screening and methods to increase caregiver disclosure of developmental concerns. The percentage of children screened has risen from under 5% prior to the onset of SS to 80% in month 18. PCPs completed 10% of screens at the onset of SS but 45% by month 18. Whereas no children were identified at risk for ASD in the year prior to SS, 18 (3.7%) children screened positively on the M-CHAT were referred for services. This percentage is comparable to those found in other Spanish language populations. Of those referred, 10 now receive services.

Conclusions: Universal screening for ASDs in primary care and successful follow-up of positive screens was facilitated by (1) assessment of community/provider needs to inform outreach, family engagement, screening, and staff training, and (2) FNs integrated into the health provider system. Attention to these issues can increase disclosure of developmental concerns by Latino families, produce positive changes in organization climate and attitudes of providers and families toward early screening and referral for ASDs, helping to reduce disparities in rates of diagnosis and treatment.

**141.130 130** The Autism Classroom Evaluation (ACE): A Tool for Evaluating Services and to Guide Training in Autism Classrooms. D. Zavatkay*[1] and S. Cleveland[2], (1)*Marcus Autism Center, Emory University*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta*

**Background:** Increasingly children with autism are being educated in specialized classrooms designed to sympathetic to the needs of this population and to address the unique cluster of symptoms. Often, educational staff lacks expertise specific to autism needed to effectively implement complex strategies recommended. Thus, a thorough evaluation tool is needed to identify strengths and needs of existing educational and behavioral services at the classroom level, to ascertain what consultation and training services are necessary, and to facilitate prioritization of the services. The Autism Classroom Evaluation (ACE) was developed to meet these needs.

**Objectives:** The purpose of this study is to validate the ACE as a tool for reliably assessing strengths and weaknesses of classroom based services for children with autism and guiding training and consultation services.

**Methods:** The ACE is used to assess aspects of classroom environment, skill acquisition programming, inclusion opportunities, and behavior management strategies in the individual classroom. Specific aspects of 12 constructs are evaluated in accordance with standards of practice for educating children with autism. All items are scored on a 5-point Likert scale yielding an average score for each construct. The ACE will be completed in 20 classrooms by educational

consultants via direct observation and staff interviews in classrooms for children with autism in both the public and private school settings. Overall results of the ACE will be presented describing the integrity of educational services available and to illustrate differences between scores obtained in classrooms with little or no outside training/consultation services and those with more extensive opportunities. **I**nter-rater, test-retest, parallel-forms, and internal consistency reliability will be assessed and results presented.

**Results:** Preliminary data suggest that overall classroom environment and scheduling appear to be relative strengths. It seems that the majority of classrooms are organized and uncluttered with appropriate areas designated for differing education and leisure activities. The weakest areas were seen when evaluating NET/generalization/maintenance programming, inclusion opportunities, and using data to track skill acquisition. In addition, across all levels behavior assessment and management were significant weakness areas. Data collection and analysis was a significant deficit in almost all classrooms observed. Data collection was not only inconsistent, it was non-existent.Preliminary data have also shown that the ACE differentiates between classrooms that have received more intense consultation and training services from those that have not across all domains. This indicates a strong need for additional training and consultation for educational staff. Additional data are being gathered in order to more fully establish the reliability of the ACE and viability of using this tool to evaluate programs and to guide consultative services.

**Conclusions:** The data show that this form is a valuable tool to assess quality of the services provided in classrooms being designed for children with autism and as a tool to guide the consultation and training of the educational staff. Additional data will show the psychometric properties of this tool to better illustrate the utility of its use and subsequent improvements in educational services for children with autism.

**141.131 131** The Experience, Accommodations, and Resilience of Grandparents of Grandchildren with Autism Spectrum Disorders. J. Hillman*[1], C. M. Anderson[2], A. R. Marvin[2], S. N. Levin[2], J. K. Law[2] and P. A. Law[2], (1)*Penn State Berks*, (2)*Kennedy Krieger Institute*

**Background:**

With increased prevalence of childhood ASD, greater numbers of adults are likely to find themselves a grandparent to a child with ASD. Although previous research has typically examined the impact of grandparents upon the adult parents of children with ASD, little is known about the experience of those grandparents themselves.

**Objectives:**

A primary goal of this study was to fill a gap in the literature regarding the unique experience of grandparents of grandchildren with ASD, from their first person perspective. In accord with resilience theory, it is essential to examine grandparents' accommodations (e.g., the extent to which they make contributions toward their ASD grandchild's general, special, and instrumental needs, and make life choices to support their grandchild) as well as perceptions of familial conflict and concern. Such knowledge will help guide the development of more effective interventions for family members affected by ASD.

**Methods:**

Participants were asked to complete anonymously an online survey designed to be completed in approximately 30 minutes and deployed by SurveyMonkey. Participants were recruited via the Kennedy Krieger Institute's Interactive Autism Network's (IAN) Research e-newsletters and the IAN Community website, along with the assistance of the Autism Speaks Foundation, the Grandparent Autism Network, and the American Association of Retired People (AARP).

Criteria for inclusion required participants to live in the U.S. and its territories, and to have at least one grandchild with an ASD. The grandchild had to be the biological, adoptive, or stepchild of the respondent's biological or adopted son, stepson, daughter, or stepdaughter.

**Results:**

A total of 1881 participants completed the on-line survey, including 1534 grandmothers (81.6%) and 347 grandfathers (18.4%), who also identified as maternal (63.4%) and paternal (35.6%) grandparents. In terms of grandparental status, more than half of the respondents were

maternal grandmothers (52.3%) followed by paternal grandmothers (29.2%), maternal grandfathers (11.9%), and paternal grandfathers (6.5%).

Results indicated that grandparents made significant accommodations and provided support toward their grandchild's general, special (e.g., Applied Behavioral Analysis; OT; educational programming), and instrumental needs (e.g., babysitting and transportation). Nearly half of the grandparents reported making personal sacrifices to help support their ASD grandchild including putting off their own retirement, becoming their grandchild's primary babysitter, and combining households. Maternal grandparents were more likely to provide instrumental care and make personal sacrifices than paternal grandparents, whereas grandfathers were more likely to provide financial support for their grandchild's special needs than grandmothers. In accord with resilience theory, the majority of grandparents reported that they were coping fairly or very well in relation to their grandchild's ASD, despite expressing significant worry for their adult son or daughter raising their grandchild. Grandparents also reported, on average, experiencing little family conflict in relation to their grandchild's ASD. Approximately 10% of the grandparents did, however, report that they were not coping well with their grandchild's ASD.

**Conclusions:**

Grandparents of grandchildren with ASD appear, on average, to be resilient and make significant accommodations on behalf of their family. Addressing the needs and experience of those grandparents would likely benefit all family members.

**141.132 132** The Experiences Impacting on the Quality of Life of Mothers of Children with Intellectual Disability and Autism Spectrum Disorder: A Qualitative Study. J. Fairthorne*[1] and C. Fisher[2], (1)*Telethon Institute for Child Health Research*, (2)*University of Western Australia*

Background:

Research has identified that mothers of children with autism spectrum disorder (autism) and intellectual disability (ID) have a lower Quality of Life (QoL) than other mothers.

Objectives:

We aimed to:

- explore QoL in mothers of children with autism and ID
- identify the factors which impacted their QoL
- document the mothers suggestions of services to improve their QoL

Methods:

Hermeneutic phenomenology provided the framework for this qualitative study. Sixteen mothers of 11-24 year old children with autism and ID undertook in-depth interviews of approximately one hour. Individually, the first author asked mothers open-ended questions pertaining to their lived experience of caring for their child or children with autism and ID. The mothers were also asked to reflect on how they considered their QoL might be and might have been improved. To elicit the essences of their experiences, their responses were analysed for significant statements which were clustered together into categories and abstracted to themes.

Results:

The three themes identified were *Coping with aspects of the child's disability*, *Adapting to a changed lifestyle* and *Surviving the challenges and savouring the rewards*. Challenging behaviours were most commonly described as the most difficult aspect of the child's disability. Adapting to a life consumed by disability and increased social isolation were the most frequently difficulties of the mothers' changed lifestyle. Most often, surviving the challenges involved detriments to employment, health and relationships. Rewards enjoyed by mothers stemmed from their love for their child, their own personal development, their child's progress and their increased opportunities to meet exceptional people. Suggested services to improve QoL in these mothers included access to meditation courses, regular comprehensive sitter services and an informal mentoring scheme. At the time of diagnosis, parents might be provided with a directory which detailed services in the state of residence and information about the disorder.

Conclusions:

Mothers of children with autism and ID experience a range of factors that impact their QoL. To ensure that they are best supported to continue their important role and enjoy an improved QoL, their lived experience and suggestions must be recognised in the planning of all support services and interventions.

**141.133 133** The High School Experiences of Adolescents with ASD - Perspectives from Multiple Stakeholders. S. Kucharczyk*[1], J. Redding[2], C. K. Reutebuch[3] and S. Hedges[4], (1)*University of North Carolina - Chapel Hill*, (2)*Vanderbilt University*, (3)*The University of Texas at Austin*, (4)*UNC Chapel Hill*

**Background:** As a whole, the public school system is falling short of its responsibility to prepare students with ASD for a productive and independent life after high school (Taylor & Seltzer, 2010). When young adults with ASD leave high school, "nearly 80% still live at home, almost half have no jobs or postsecondary training, 40% never have contact with friends, 17% never feel hopeful about the future, 21% never engage in outside activities, and many experience a decrease in insurance coverage and therapy services" (Shattuck, 2010). Gathering and acknowledging the perspectives of stakeholders directly involved in the education and experience of high school students with ASD is essential to implementing effective interventions that address this shortfall and offer more promising outcomes.

**Objectives:** This study examines the perspectives of stakeholders involved in the education of high school students with ASD on the following issues: (1) how the transition-related needs of adolescents with ASD are currently being addressed, (2) what considerations and challenges arise when implementing interventions for adolescents with ASD, and (3) what professional development, resources, and supports are needed to address the transition-related needs of adolescents with ASD well.

**Methods:** Focus group methodology was used to gather data across multiple stakeholders (i.e., family members, adolescents and young adults with ASD, educators, administrators, community members, service providers) and regions of the United States (i.e., South, Midwest). A total of 152 participants attended the 28 focus group sessions across 4 states (i.e., North Carolina, Tennessee, Texas, and Wisconsin). The largest stakeholder groups represented were parents ($n$ = 47) and educators ($n$ = 45), and the smallest number represented individuals on the spectrum ($n$ = 6). Other groups were school administrators ($n$ = 24) and service providers/community members ($n$ = 24). Data was analyzed through a multi-step, team-based approach using NVivo10 software (QSR International, 2012) to code, categorize, and capture emerging themes.

**Results**: Three distinct themes emerged from the analysis of focus group participants: (1) efforts made by schools to address the needs of youth with ASD are for the most part insufficient or nonexistent; (2) the feasibility of interventions for adolescents with ASD (e.g., time and effort required, buy-in) and the variability of ASD are inhibitors to implementation and sustainability; and (3) the need for professional development, resources, and support is critical.

**Conclusions:** Improvement in post-secondary outcomes for individuals with ASD will require a comprehensive effort across high schools to enable them to be proactive in addressing behavior, academic, and social problems; enhance instruction; better support individuals with ASD and their families in high school and beyond; and enable students to reach their full potential. Implications on the development of interventions, professional development, and related research grounded in the perspectives of stakeholders will be discussed.

**141.134 134** The Importance of Explaining Autism to Peers for Promoting Social Inclusion and Interaction in Mainstream School Classrooms. P. Molteni*[1], L. d'Alonzo[1] and M. Colombo[2], (1)*Università Cattolica del Sacro Cuore*, (2)*Ufficio Scolastico Regionale per la Lombardia - Ufficio XVIII Monza e Brianza*

*Background:* Italy has a long history of inclusion of students with autism in mainstream schools but there is no research evidence on the experience and impact of explaining autism to peers. Indeed, peer interaction and friendship is fundamental to support inclusion and learning processes (DeRosier et al., 2011). The present research investigates how teachers help peers in understanding the condition, enabling them to interact with their mate, and how awareness activities have to be designed and implemented in a proper coordinated manner, considering students' age and school setting (Feldman et al., 2013).

*Objectives:* The research aims to analyse the importance of explaining autism to peers in mainstream schools and its impact on classroom inclusion and social relationships quality. The research questions are: i) Why and how often do teachers plan specific peer-to-peer activities?; ii) Are teachers aware of the importance of explaining autism to peers?; iii) Which insights do teachers have in explaining autism to peers?; iv) Which positive consequences do occur in peers interaction after explaining autism?

*Methods:* This research was designed as a pilot study that involves a multi-methods approach, including Action and Collaborative Research Methodology. The designed research allows the researcher to catch the complexity of a province school district (from kindergarten to high school) through a deep detailed analysis of selected aspects. The researcher explored the questions described above through observations (10), questionnaires (133) and focus groups (2). The qualitative and quantitative data collected during the research were analysed using the Interpretative Phenomenological Analysis (IPA).

*Results:* Explaining autism to peers is fundamental to support class interaction and friendships in inclusive mainstream schools, since the kindergarten. The research underlines: how teachers promote small group interaction instead of large groups activities involving the student with autism; how teachers working in kindergartens and high schools are not aware of the importance of explaining autism to peers; how the students' group can positively benefit by understanding the classmate with autism; how, after the explanation, there is an significant increase of positive interaction with the student and toleration of his/her challenging behaviours.

*Conclusions:* As this research as shown, promoting and enhancing the importance of explaining autism to peers is fundamental to enable mainstream schools teachers to define educational and life-long plans able to properly answer the group's needs and support the student's real inclusion in the classroom. This study is a good example of how the educational research can meet and help the daily practice in working with people on the autism spectrum and promote good practice of mainstream school teachers: the results will support the implementation of new class intervention and tools for raising professionals and peers' awareness.

**141.135 135** The Relationship Between Age, Severity, and Services for Children with ASD. S. Goldman*[1], M. P. Mello[1], R. C. Urbano[2] and R. M. Hodapp[1], (1)*Vanderbilt University*, (2)*Vanderbilt Kennedy Center*

**Background:** Although the diagnosis of autism spectrum disorder (ASD) involves atypical social interactions, communication deficits, and restricted or stereotyped behaviors, children with ASD also show other, co-occurring behavior problems. Unfortunately, little is known about how these co-occurring symptoms should inform targeted interventions for these children and how these interventions might vary by age. Compared to children with other disabilities, children with ASD often receive a high number of services with a lack of a standardized treatment approach.

**Objectives:** This study examines how service receipt changes over age and whether services are tied to the presence or severity of specific behavioral problems

**Methods:** Respondents included 361 parents of children ages 2-21 with ASD who completed an online survey. Children had a mean age of 10.02 years (SD = 5.12) and received an average of 3.40 (SD = 2.13) services (range from 0 to 10 services). Parents reported a mean behavior problem severity score of 2.43 (with 1 = no problem and 4= severe problem) on 12 behavior items from the Parental Concerns Questionnaire (McGrew et al., 2007).

**Results:** Factor analysis with varimax rotation was first performed on these 12 behavior items and two factors were extracted. The first, named *Psychiatric Behaviors*, explained 27.19% of the variance and the second, named *Autism Characteristics*, explained an additional 22.78%. A 2x2 ANOVA was then performed for service provision by age group (age 2-9 and 10-21) for the *Psychiatric Behaviors* and *Autism Characteristics* factors. Results showed that those receiving Special Education, PT/OT, Health, and Respite had higher scores on the *Autism Characteristics* factor, regardless of age group. There was also a significant interaction ($p<.05$) between Speech and age group. For the *Psychiatric Behaviors* factor, there was a significant relationship with age for Special Education, Health, Counseling/Psych, and Respite

services, with a significant interaction ($p<.05$) between service provision and age for Speech and Behavior Support services.

**Conclusions:** Results show a relationship between some commonly co-occurring behavior problems reported for children with ASD. These two factors, *Psychiatric Behaviors* and *Autism Characteristics*, may be useful in linking need to service and making decisions about important supports for children with ASD. Our results also support the idea that treatments vary by age group, across disability severity (Green et al., 2006). Future research should confirm the reliability of parental reporting with professional reports of behavior problems and services.

**Key References:**

Green, V. A., Pituch, K. A., Itchon, J., Choi, A., O'reilly, M. & Sigafoos, J. (2006). Internet survey of treatments used by parents of children with autism. *Research in Developmental Disabilities, 27,* 70-84.

McGrew, S., Malow, B. A., Henderson, L., Wang, L., Song, Y. & Stone, W. L. (2007). *Developmental and behavioral questionnaire for autism spectrum disorders. Pediatric Neurology, 37,* 108-116.

**141.136 136** The UK ASD+ Study: Co-Existing Conditions of Children with ASD, Unmet Needs for Services and Impact on the Family.

B. Koshy*[1], J. Rodgers[2], A. S. Le Couteur[2], H. McConachie[3] and J. Parr[2], (1)*Institute of Neuroscience, Newcastle university*, (2)*Newcastle University*, (3)*Institute of Health and Society, Newcastle University*

Background:

Children with autism spectrum disorder (ASD) have multiple co-existing emotional and behavioural conditions ranging from disorders of sensory perception to psychiatric co-morbidities. These co-existing conditions add a significant burden to the care of children with ASD.

Objectives:

- To identify the prevalence of parent/carer–reported unmet needs regarding support for co-existing conditions in children with ASD
- To understand the interactions between co-existing emotional and behavioural conditions, parents' unmet needs regarding the services received and the impact on family.

Methods:

Parents were recruited from either the population-based Database of children with ASD living in the North East of England (Dasl[n]e), or a research register - the Autism Spectrum Database – UK (ASD-UK). 630 families responded to a postal survey that included parent report questionnaires about co-morbid psychopathology (ASD-CC – Autism Spectrum Disorder Comorbidity – Child Version) and problem behaviour (ASD-PBC – Autism Spectrum Disorder Problem Behaviour – Child Version) in children. Questionnaires about parents' unmet needs, and Impact on Family (IOF) were also completed. ASD-CC and ASD-PBC were used to define co-existing emotional and behavioural conditions. The parent questionnaire on unmet needs was developed with the help of parents of children with ASD and covered services received in relation to feeding, sleep, anxiety, hyperactivity, other behavioural problems and sensory issues.

Results:

More than two-thirds of families had at least one unmet need; only 30% of families had their needs for support for managing co-existing conditions fully met. Parents of children with moderate to severe impairment in co-existing emotional and behavioural conditions (as defined in the ASD-CC), had greater unmet needs than parents of children with no/minimal impairment (2.96 vs. 1.51; $p=.000$); they also reported greater impact on the family (45.45 vs. 35.39; $p=.000$).

Two linear regression models were built with total unmet needs and impact on the families as the criterion variables. For unmet service needs, total co-existing emotional and behavioural conditions ($\beta=.440$; $p=.000$) and younger age ($\beta=.132$;$p=.003$) contributed significantly to the model while type of diagnosis, gender, language level, school type and sibling/s with ASD did not make a significant contribution.

For impact on the family, total co-existing emotional and behavioural conditions ($\beta=.513$; $p=.000$), total unmet needs ($\beta=.155$; $p=.000$), siblings with ASD ($\beta=.089$; $p=.015$) and type of ASD diagnosis ($\beta= -.082$; $p=.033$) contributed

significantly to the model while age, language level and type of school made no significant contribution.

Conclusions:

Co-existing emotional and behavioural conditions had a direct significant impact on the family. Unmet service needs had an amplifying effect on this relationship. Improving support/intervention services for parents of children with ASD and co-existing emotional and behavioural conditions is necessary in an attempt to reduce the impact of these conditions on family life.

**141.137 137** Validity and Reliability of the Parent Activation Measure for Developmental Disabilities. L. A. Ruble*[1], D. S. Murray[2], K. Brevoort[3], V. Wong[1] and J. McGrew[4], (1)*University of Kentucky*, (2)*Autism Speaks*, (3)*Cincinnati Children's Hospital*, (4)*Indiana University-Purdue University*

Background:

Individuals with ASD are high users of medical services costing about $35 billion annually. Surprisingly, very little is known about the interactions between caregivers of children with ASD and their healthcare providers. Because high quality care is associated with informed decision-making, ways to assess and improve the knowledge of consumers concerning their healthcare problems is critical. "Activation" is one term used to operationalize consumer-directed healthcare decision-making. Consumers who are "activated" with skills, knowledge, and motivation are more effective in healthcare management. The objective of this pilot work was to develop a sensitive, valid, and reliable measure of parent activation so that we have effective ways to assess whether interactions with healthcare providers are based on activation and to determine whether activation was associated with decreased parent stress and improved self-management of their child.

Objectives:

1. To evaluate the reliability of a method of assessing parent activation.

2. To evaluate the associations between parent activation, parent stress, and parent self-management regarding their child.

Methods:

Thirty-six parents of chldren with autism spectrum disorder between 3 and 12 years and who received a Therapeutic Programming Session (TPS) were asked to participate. TPS is a model of outpatient multidisciplinary service based on collaborative parent-child service planning and decision-making developed at the Kelly O'Leary Center for Autism Spectrum Disorders at the Cincinnati Children's Hospital. The aims of TPS are to identify parent concerns, assist parents in obtaining services based on parent priorities and concerns and provide direction for navigating the complex service system. Parents participating in TPS were invited to complete the Parent Activation Measure for Developmental Disabilites (PAM-DD) one week prior to their initial visit. The PAM-DD is anew 13-item questionnaire tested for this study assessing parent knowledge, skill, and confidence for self-management of their child. It was based on Hibbard et al., (2005) Patient Activation Measure. Parents also completed the Parenting Stress Index- Short Form (Abidin 1990) and an in-house self-management assessment (SMA) of how certain they are that they can manage their child's sleep, behavior, eating, toiling, and school issues using an 11-point Likert Scale ("0" not managing at all to "10" managing well). All measures were given 1-week before their TPS.

Results:

The internal consistency of the PAM-DD as measured using intraclass correlation was good (alpha = .80). As expected, the PAM-DD correlated negatively with parent stress ($r = -.52$, $p = .002$) and positively with self-management of child's problems ($r = .52$, $p = .006$).

Conclusions:

Overall, initial findings suggest that the PAM-DD is a valid and reliable tool that is sensitive to variation in parent stress and self-management and could serve as an important tool to assess the quality of parent-provider healthcare interactions.

**141.138 138** Young People with Complex Health Needs: Baseline Data from a Longitudinal Study of Transition from Child to Adult Healthcare Services. A. S. Le Couteur*[1], H. Merrick[1], H. McConachie[2], K. D. Mann[1], J. Parr[1], A. Colver[1] and .. Transition Team*[3], (1)*Newcastle University*, (2)*Institute of Health and Society, Newcastle University*, (3)*Newcastle Univeristy*

Background:

Many young people (YP) with complex health needs (CHN) have poor health and social outcomes following transition from child to adult health services. The influence of transitional care on the wellbeing of young people with CHN and the need to ensure smoother transition processes is recognised in much recent health policy. However, there are limited satisfaction and health outcome data to support proposed models of care.

Objectives:

This 3-year longitudinal study aims to identify the features of transitional care that are acceptable, and potentially effective and efficient for YP with CHN making their health service transition. Here we present the baseline data showing how the experiences of services, participation, and feelings of wellbeing compare between YP with autism spectrum disorder (ASD) with additional mental health problems, YP with cerebral palsy (CP) and YP with diabetes. The literature suggest that transition services in diabetes are better developed than those for YP with CP or ASD; therefore it is hypothesized YP with diabetes will report better experiences with services and greater participation.

Methods: 355 YP aged 14 years to 18 years 11 months have been recruited to this longitudinal study. YP have completed questionnaires on wellbeing (Warwick-Edinburgh Mental Wellbeing Scale), participation (Rotterdam Transition Profile), and satisfaction with services (Mind the Gap).

Results:

No differences across groups in the YP's satisfaction with services were found. However, parents of YP with CP or ASD reported significantly lower satisfaction with service *process issues* than parents of YP with diabetes. When parent scores were matched and compared to that of their YP, parents reported significantly lower satisfaction with *provider characteristics* and *process issues*. YP with diabetes reported greater levels of independence in participation than those with CP or ASD in the majority of domains, including household responsibilities ($p=0.001$), social activities ($p<0.001$) and decisions about healthcare needs ($p<0.001$). YP with ASD reported significantly lower wellbeing scores than those with CP or diabetes ($p<0.001$).

Conclusions:

The YP in all groups reported similar experiences of services but significantly greater satisfaction with the process of care and the provider's interpersonal style than their parents. Regarding participation, the YP with diabetes have made greater progress in their planning for adult healthcare and independent skills, compared with YP with CP or ASD . The study will continue to track relationships between YP's experience of transitional health care and influences on their wellbeing and participation over the next three years.

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***Transition Team: A, Bilson., S, Bruce., T, Cheetham., Z, Huma., C, Maiden., J, Milne., J, Owens., J, Parkes., M, Pearce., N, Thalange.**

## 142 Other Topics

**142.139 139** A Technical Demonstration of Rexdb, an Open Source, Integrated Data Management Platform for Autism Research. C. H. Tirrell*, D. Voccola, L. Rozenblit, C. C. Evans, O. McGettrick, O. Golovko and F. Farach, *Prometheus Research, LLC*

Background: RexDB is an open source, integrated data management platform for the collection, integration, curation and exploration of human biomedical and translational research. Its extensible, web-native platform can be used to help researchers securely integrate, manage, query and share their behavioral, medical, genomic, imaging and biospecimen-inventory data from multiple studies. After several previous development iterations used to deliver data management solutions for a wide range of studies in autism and associated disorders research, Prometheus Research decided to open source all aspects of the RexDB research platform for the greater scientific community. This open sourcing initiative began in 2011 with a completely new redesign of all elements of this platform.

Objectives: The objective of this presentation is to demonstrate to potential users of the RexDB platform its core functionality. It will cover the basic configuration of a research study and its instruments, entering data regarding research subjects and their participation in complex studies, and the exploration of the resulting data for use in creating datasets for analysis. Users will be given instructions on how to download, install and launch the RexDB platform and configure it for a simple study for autism study.

Methods: The RexDB platform is divided into four core functional software modules comprised of numerous individual components; RexPlatform, RexAcquire, RexIntegrate and RexPlore.

RexPlatform is a toolkit that enables the installation of all necessary software for hosting, building and extending a RexDB instance. It contains a thin data-access layer called RexQL and tools used to deploy database schemas, conduct ETL (Extract, Transform and Load) operations and rapidly build screen interfaces.

RexAcquire is a comprehensive Electronic Data Capture (EDC) platform that includes mechanisms to directly capture data from various clinical informants, as well as a duel-data validation entry system designed for rapid keyboard entry by clinical staff members.

RexIntegrate is used to help researchers securely integrate, manage, query and share their behavioral, medical, genomic, imaging and biospecimen-inventory data. It contains a study management data structure to manage the complexities of single visit or longitudinal studies.

RexPlore enables users to create custom, shareable data sets from RexIntegrate that will allow them to explore and understand their research data. It allows them to summarize, visualize, and statistically analyze their form, participant, study and biospecimen research data within the product and export the results to numerous third-party tools, such as Excel, SAS, SPSS or R.

Results: The RexDB software platform has been used to deliver solutions for integrated data management needs of individual laboratories conducting single studies to large-scale autism research initiatives covering multiple sites conducting multiple studies utilizing multiple research instruments. This platform has enabled groups that have significantly impacted the autism research space, such as the Simons Foundation, Autism Speaks and the Marcus Autism Center, to manage their complex data collection, integration and analyzation needs.

Conclusions: The open sourcing of this platform will afford autism researchers the opportunity to more easily collect and share their results across the entire field of research.

**142.140 140** An Effective, Scalable Privileging Model for Enabling HIPAA-Compliant User Access in a Shared Data Repository.

D. Voccola[1], A. Van Wagner*[1], C. H. Tirrell[1], T. Cermak[2], M. Yourd[1] and W. Jones[3], (1)*Prometheus Research, LLC*, (2)*Marcus Autism Center*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

**Background:** Multiple factors are causing an increase in the need for both local and multi-site collaboration in autism research (OARC/IACC, 2012). This increased need, while arguably beneficial in a still-emerging research domain, such as autism, often produces significant unanticipated problems for collaborators: (1) They typically lack access to research informatics expertise, resulting in homegrown re-creations of appropriate (read: HIPAA-compliant) data access rules; and (2) their usual "data" tools (e.g., Excel, SPSS, R, Access) are not designed to facilitate the enforcement of these rules.

**Objectives:** Suggest a relational data model and set of cascading data access rules for creating a shareable data repository capable of complying with all relevant sections of HIPAA's Administrative and Technical Safeguards using a newly available database tool.

**Methods:** We interviewed investigators, clinicians, and research staff at the Marcus Autism Center and Emory University about their perceived needs and challenges in the areas of security and convenience when sharing data in a collaborative environment. We designed two solutions, each containing sets of cascading data access rules accounting for each of the major components in determining "minimum necessary" data access for a given research team member, and a complimentary relational data model for

configuring and enforcing these rules. Solution 1 assumed a sharing-centric institutional environment in which cooperative agreements exist between investigators, facilitated by the use of consistent participant consent language between projects (à la Marcus). Solution 2 assumed a project-centric (a.k.a., "siloed") environment, in which consent language and data sharing agreements can vary widely, even within the same institution. Using the default Research Exchange Database (RexDB) schema as our starting point, we designed and tested several data model augmentations and calculated rule-sets, which were presented back to the interviewees.

**Results:** Solution 1 was accepted for deployment at the Marcus Autism Center. When launched near the end of 2013, it will automatically enforce "minimum necessary" data access for nearly 100 users across several overlapping research cores and projects at the Center.

**Conclusions:** Researchers need not design homegrown solutions to solve the perceived challenges of data access in an increasingly collaborative landscape. Most data access permutations can be appropriately addressed by a small set of pattern-based data access rules. These rules can be applied and configured using available data management software, such as RexDB.

**Citation:**

Office of Autism Research Coordination (OARC), National Institute of Mental Health and Thomson Reuters, Inc. on behalf of the Interagency Autism Coordinating Committee (IACC). IACC/OARC Autism Spectrum Disorder Research Publications Analysis Report: The Global Landscape of Autism Research. July 2012. Retrieved from the Department of Health and Human Services Interagency Autism Coordinating Committee website: http://iacc.hhs.gov/publications-analysis/july2012/index.shtml

**142.141 141** Service Delivery Processes and Parenting Stress Among Families of School-Aged Children with ASD.

A. Zaidman-Zait*[1], P. Mirenda[2], P. Szatmari[3], S. E. Bryson[4], E. Fombonne[5], T. Bennett[6], E. K. Duku[6], M. Elsabbagh[7], S. Georgiades[6], I. M. Smith[8], W. Roberts[3], T. Vaillancourt[9], J. Volden[10], C. Waddell[11], L. Zwaigenbaum[10] and A. Thompson[6], (1)*Tel-Aviv University*, (2)*University of British Columbia*, (3)*University of Toronto*, (4)*Dalhousie/IWK Health Centre*, (5)*Oregon Health & Science University*, (6)*Offord Centre for Child Studies & McMaster University*, (7)*McGill University*, (8)*Dalhousie University / IWK Health Centre*, (9)*University of Ottawa*, (10)*University of Alberta*, (11)*Simon Fraser University*

Background:

Autism Spectrum Disorder (ASD) presents a wide range of challenges for which families seek professional support across the lifespan. Parents also experience high levels of stress that is chronic and persistent over time (Zaidman-Zait et al., 2013). Thus, treatments and supports for families of children with ASD should address the needs of the entire family. The provision of family-centered services (FCS) has been shown to be associated with higher levels of parental satisfaction and better parental and child psychosocial well-being in non-ASD populations (King et al., 2004; Rosenbaum et al., 1998).

Objectives:

This study sought to examine (1) parents' perceptions of the extent to which the after-school treatment services their children with ASD received were family-centered, over a 12-month period; and (2) the relationship between parents' perceptions, child service utilization, and parenting stress over a 12-month period, after controlling for child behavior problems.

Methods:

Data were drawn from the Canadian Pathways in ASD study and included 124 parents and their children with ASD, who were 7-8 years old at T1 (mean age = 7.75 years). Data were available 12 months later (T2) for 82 of these families, when the children were aged 8.7 years, on average. At both time points, parents completed a family demographic survey; the Measure of Processes of Care (MPOC-20; King et al., 2004); and the Community Program Services and Activities questionnaire (Brayson et al., 2009). At T2, parents completed the Parenting Stress Index-Short Form (PSI-SF) and the Child Behavior Checklist 1.5-5 (CBCL). Teachers also completed the CBCL at T2.

Results:

Profile analysis results indicated that, at T1, mean scores on the MPOC subscales related to providing general information (M = 4.18) and enabling

partnerships with families (M = 4.83) were lower than scores on the other three subscales (i.e., providing specific information about the child, providing coordinated and comprehensive care for the child and family, and providing respectful and supportive care). Paired t-tests indicated that, over a 12-month period, there was a significant increase in scores on the enabling partnerships subscale ($t$ = -2.28, $p$ = 0.02). In the regression analysis, parent and teacher child behavior problem scores on the CBCL at T2 were entered in the first block, and accounted for 23% of the variance in parenting distress ($F$=17.85, $p$<.001). The average number of after-school treatment hours at T1 and scores on the two MPOC information-providing subscales were entered in the next two steps, with no significant effects. Scores on the three MPOC subscales addressing supportive care and parent–professional relationships were entered in a final step, and accounted for an additional 14% of the variance in parenting stress at T2. The overall model explained 38% of the variance in parental distress on the PSI-SF at T2 ($F$ = 4.72, $p$<.001).

Conclusions:

Service delivery processes make an important contribution to parents' experiences of stress. Professionals providing interventions to school-age children with ASD should endeavor to build supportive and collaborative relationships with families. Such relationships may help to ameliorate parenting stress over time.

**142.142 142** How Does a Western Approach to Autism Work within a Chinese Population? Service Provision for Children with Autism Spectrum Conditions in Hong Kong. X. Sun*, C. Allison, B. Auyeung, S. Baron-Cohen and C. Brayne, *University of Cambridge*

Background: As a British colony between 1842-1997, Hong Kong (HK) adopted a British healthcare system. Originally part of mainland China, HK is thus a unique region in which Western and Eastern cultures combine to influence a small island. This affords an opportunity to examine how autism is recognized, understood, and supported, in a unique cultural context. Previous research in mainland China suggested underdeveloped services and delays in recognition of Autism Spectrum Conditions (ASC) partly due to certain beliefs about child development rooted in Chinese culture, such as late language being a positive attribute of a child. The cultural context of service provision for autism has not previously been explored in HK.

Objectives: (1) To investigate patterns of service provision for children with ASC in HK; (2) To investigate whether similar cultural issues found in mainland China also exist in HK.

Methods: Parents in the largest non-governmental organization in HK for preschool children with ASC were invited for participation. Thirty-four in-depth interviews were conducted using a semi-structured questionnaire (50 questions: from first awareness to intervention) developed from previous interviews in mainland China. Using a framework approach, seven themes were identified to summarize difficulties and perceptions into service development: 1) awareness and knowledge of ASC; 2) parenting patterns; 3) acceptance of diagnosis; 4) diagnostic confusion; 5) frustration along the pathway; 6) expectations of support; and 7) parental concerns.

Results: The identification and diagnostic service for ASC in HK uses a combination of early screening and multi-disciplinary assessments, based on a UK model. However, the majority of children were identified by parental initiation of referral (56%) and other check-ups (29%) rather than via screening. The mean age of children at first awareness of atypical development was 1.8 yrs (range: 1.4-3). There was a delay in diagnostic referral. Similar to mainland China, 17.7% families considered language delay a sign of child's future success and did not seek help until later. The mean interval from first awareness to diagnosis was 9.3 months (SD = 6.9). The diagnostic process took an average of 4.6 months (SD = 4.5). Regarding intervention, children under 6 with ASC are entitled to receive intervention in government-supported non-profit rehabilitation centres. However, the mean time on the waiting list entering such centre was 14.8 months (SD = 5.4). More than half of the parents (56%) had never attended parent training courses to learn how to help their children outside the classroom. Similar to mainland China, there were no specific facilities for children with ASC older than 6.

Conclusions: Although adopting a more Western approach, this study highlights a perceived lack of professionals and rehabilitation services for ASC in

HK, leading to long waiting times for services. Due to lack of knowledge of ASC, less than half of parents actively seek help, other than waiting. Although Western culture and system was adopted, similar cultural issues found in mainland China also exist in HK, which contribute to delays in the recognition of ASC. Further service development needs to be sensitive to the cultural context.

**142.143 143** Men Are from Mars, Women Are from Venus: 2D:4D Digit Ratio Mediates Emotion Recognition from Male Eyes in Men. N. Brondino*, T. Veglia, U. Provenzani, M. Besozzi, L. Folini, E. Caverzasi, F. Barale and P. Politi, *University of Pavia*

Background: according to the theory of gender differences in cognitive styles, the male brain is more preprogrammed to construct and comprehend systems based on logic rules, while the female brain is more hardwired to understand other people's mental states and emotions. It has been suggested that androgen (especially testosterone) prenatal exposure may effect brain development towards a more male-typical cognitive style. In this regard, the ratio of the length of the index finger to the ring finger (2D:4D digit ratio) is generally considered a measure of prenatal androgen exposure, as low 2D:4D digit ratio has been associated with high fetal testosterone. To date, there are controversial data on the correlation between 2D:4D digit ratio and emotion recognition.

Objectives: the present study aimed to investigate the potential correlation between emotion recognition and 2D:4D digit ratio in a cohort of healthy young adults.

Methods: one hundred and fifty subjects were recruited. All participants were screened by a senior psychiatrist to exclude the presence of psychiatric disorders. Participants completed the Autism Spectrum Quotient (AQ), a measure for the identification of autistic traits in the general population, the Empathy Quotient (EQ) and The Reading the Mind in the Eye Test (RMET), both measures of empathizing.

Results: in the entire sample, there was a significant correlation between left 2D:4D digit ratio and number of RMET correct responses. Analyzing data by gender, women showed more empathizing qualities compared to men ($p<0.001$) and displayed a higher number of RMET correct responses both to female and to male eyes ($p<0.001$). However, no significant correlation between 2D:4D digit ratio and number of RMET correct responses was observed in women. In male subjects, we observed a significant positive correlation ($p<0.01$) between left 2D:4D digit ratio and number of RMET correct responses to male eyes.

Conclusions: these preliminary results are in line with the hypothesis that females outperformed males in empathizing. Interestingly, literature data reported that men have more difficulties to recognize emotional expressions in female as compared to male eyes and emotion recognition in male eyes has been associated with an increased right amygdala response. Our results may suggest that androgen priming of the brain (as expressed by 2D:4D digit ratio) might be a mediator for this effect.

**142.144 144** Conditional Probabilities of Dynamic Visual Scanning in School-Age Children with ASD. A. Khan*[1], S. Shultz[2], W. Jones[3] and A. Klin[3], (1)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*

Background: When viewing scenes of naturalistic social interaction, individuals with Autism Spectrum Disorders (ASD) allocate visual attention differently than typically-developing (TD) children. However, studies have not examined the *temporal* sequence of fixations: how the probability of a current fixation location depends on prior fixations. Fixating on a given location at one moment in time may result in learning that impacts where one looks in the future. Likewise, a failure to fixate on that location may result in different future fixations. Examining the temporal sequence of fixations may reveal what is learned or what is missed by children with ASD when viewing scenes of social interaction.

Objectives: This study aims to: (1) identify, within movie scenes of social interaction, onscreen fixation locations that strongly predict future fixation locations in TD children; (2) identify fixation locations that strongly predict future fixations in children with ASD; and (3) measure whether fixation locations predict the same or different future fixations in children with ASD compared to TD children.

Methods: School-age children with ASD (n=26) and TD children (n=23) were matched on chronological age and verbal IQ. Children watched videos of age-appropriate social interaction while eye-tracking data were collected. Our analysis focused on fixation locations perceived as highly salient to viewers (as indexed by timepoints when the majority of viewers looked at the same location). These fixation locations were identified separately for TD and ASD groups (referred to as 'TD targets' and 'ASD targets'). To determine whether the probability of fixating on a current target depends on fixation on a prior target we calculated probability ratios: the proportion of viewers who fixated on target X *and* target X-1 relative to those who fixated on target X but *not* X-1). Probability ratios were calculated for all pairs of targets identified by TD viewing patterns (aims 1,3) and for all pairs of targets identified by ASD viewing patterns (aim 2).

Results: Aim 1: Preliminary results show that in TD viewers, 59.5% of TD targets showed higher conditional dependency than expected by chance ($p<.05$). This indicates that 59.5% of the targets fixated by TD children were *more likely* to be fixated *if* those children had looked at specific locations earlier in the movie, but were *less* likely to be fixated if those children *had not* looked at those earlier locations. Aim 2: By contrast, in ASD viewers, 38% of ASD targets showed higher conditional dependencies than expected by chance ($p<.05$). Aim 3: In ASD, the probability of fixating on a TD target did not depend on viewing prior TD targets, suggesting that both groups arrive at the same target location via a different pattern of prior fixations.

Conclusions: In navigating the social world, current insights depend on past experience. Failure to learn about information conveyed in certain locations may result in later visual fixations that are more divergent from normative viewing patterns. Studies examining the temporal sequence of fixations offer important insights into visual scanning strategies in children with ASD, and the way in which those strategies shape subsequent learning.

## 143 Hyper or Hypo? Towards an Integrative Model of Network Connectivity in ASD

*Discussant:* R. T. Schultz *The Children's Hospital of Philadelphia*

*Organizer:* R. A. Müller *Dept. of Psychology, San Diego State University*

The functional connectivity literature on ASD has grown exponentially in the past decade, but initial consensus on 'general underconnectivity' has been undermined by conflicting results and the growing awareness of methodological issues (e.g., head movement, spontaneous vs. task-driven signal fluctuations) that may have dramatic effects on findings. This panel is motivated by the need for a more nuanced and developmental understanding of functional connectivity and aims to present perspectives for a comprehensive model of network abnormalities in ASD that may reconcile the vast array of diverse and often seemingly inconsistent findings. Presentations in this panel will attempt to elucidate (i) how and why MRI findings (functional connectivity, DTI) have been divergent, (ii) how different analytic approaches can provide a comprehensive view of aberrant functional connectivity, (iii) how multimodal approaches, including electrophysiological techniques such as MEG, can contribute to more differentiated models of network abnormalities in ASD, and (iv) how differential findings may be reconciled in network-specific models that relate to core symptomatology.

**143.001** Disrupted emergence of networks in ASD: Evidence from fcMRI and DTI. R. A. Müller*, *Dept. of Psychology, San Diego State University*

Background: There is broad consensus that ASD requires investigation at the brain network (rather than local) level. Huge amounts of data, mostly from functional connectivity MRI (fcMRI) and diffusion tensor imaging (DTI), published in the past decade support abnormalities of functional and anatomical network connectivity in ASD. While quantitatively reports of underconnectivity predominate, empirical inconsistencies, methodological challenges, and conceptual issues today highlight the need for a more nuanced interpretation of findings.

Objectives: To outline a developmental model reconciling some of the most problematic inconsistencies in the fcMRI and DTI literature on ASD, based on methodological and conceptual considerations.

Methods: Exemplary findings from literature and from own fcMRI and DTI studies (including total cohorts of over 60 children and adolescents with ASD, ages 7-18 years, and an age, sex, handedness and nonverbal IQ-matched typically developing [TD] cohort) will be reviewed.

Results: FCMRI findings in ASD range from 'general underconnectivity' to 'general overconnectivity' across different studies. Factors such as participant age, head motion, and effects of global signal fluctuations have been debated, but are unlikely to provide an explanation of the inconsistencies. Other methodological factors, in particular those relating to the difference between task-driven vs. intrinsic signal correlations, account for larger amounts of variability in between-group effects, based on a literature survey as well as empirical demonstration in three independent datasets including >100 participants.

DTI results for ASD show a different pattern of inconsistencies. While findings indicating white matter compromise (e.g., reduced fractional anisotropy [FA], increased mean diffusion [MD]) predominate, regional or tract-specific patterns have varied much across studies. There are also notable exceptions of studies with inverse effects (e.g., increased FA in ASD). Most of these included infants and children under the age of 8 years.

Conclusions: Given relatively firm evidence of early with matter overgrowth in ASD, the DTI evidence from infants suggests that at some point in the first two years of life, at least some parameters of anatomical network organization (e.g., axonal numbers, myelination) progress precociously and out of step with experiential input available from emerging sensorimotor systems. This asynchrony subsequently dampens progressive and regressive mechanisms of neurotypical plasticity and the emergence of distinctly sculpted functional networks, with the result of inefficient ('noisy') information transfer. FCMRI can detect both aspects of developmental network abnormalities in ASD, with underconnectivity within neurotypical networks reflecting impaired progressive and diffuse (out-of-network) overconnectivity reflecting impaired regressive mechanisms. DTI findings in participants >8 years of age further support impaired progressive mechanisms. However, the technique's currently limited ability to resolve multiple fiber directions within a voxel make conventional DTI protocols largely insensitive to the detection of residual excessive overconnectivity.

**143.002** Local and long-range functional connectivity abnormalities in ASD: Frequency-specific insights from MEG. T. Kenet*, *Mass Gen Hosp/Harvard Med School*

Background: Functional connectivity in the brain is often modulated by cortical oscillations occurring on much faster time scales than can be measured using the BOLD signal. MEG signals are well suited for measuring these fast oscillations, and are also easily corrected for motion artifacts thanks to continuous motion tracking. Thus, MEG offers a complementary approach to fMRI for assessing functional connectivity abnormalities in ASD.

Objectives: To elucidate the nature of both local and long-range functional connectivity abnormalities in ASD with high spectral specificity, and to evaluate the links between these functional connectivity metrics and behavioral measures.

Methods: MEG data were recorded during resting state, passive tactile vibrations on fingertips, and face processing paradigms. Group sizes varied from N=15 to N=20 per group per paradigm, with some overlap in cohorts across studies. Long-range interactions were examined between functionally distinct cortical regions. Local interactions were examined within a functionally defined cortical region, i.e. on a spatial scale of the order of about one square centimeter on the inflated cortex.

Results: We found patterns of both increased and reduced functional connectivity across cortical regions in ASD in different paradigms. During resting state in particular, the properties of the network varied consistently with frequency band. In addition, two of the paradigms, tactile vibrations and face processing, also allowed us to investigate specific aspects of local functional connectivity. In contrast to the long-range functional connectivity results, for both types of stimuli and using different approaches we observed only reduced local functional connectivity in the ASD group. These long-range and local neurophysiological functional connectivity metrics correlated with ASD severity as measured on the ADOS, and in the case of the sensory task, also with behaviorally derived sensory processing scores. Lastly, blind statistical classification using these metrics achieved up to 90% accuracy in identifying ASD participants.

Conclusions: Our results support and expand on findings from fcMRI, showing the co-existence of atypically increased and reduced long-range functional connectivity in ASD. Additionally, our studies to date suggest that at least local interactions that are likely mediated via inhibitory connections are uniformly reduced in ASD. The correlations between these spectrally specific functional connectivity metrics and behavioral ASD measures suggest a relevance to the etiology of ASD.

**143.003** Toward a fine-grained characterization of the intrinsic functional connectome in ASD. A. Di Martino*[1], A. ABIDE Consortium[2] and M. P. Milham[3], (1)*NYU Child Study Center*, (2)*NYU CSC*, (3)*Child Mind Institute*

Background: While the dysconnection model of autism has been increasingly supported by direct and indirect evidence from diverse fields of neuroscience, a fine-grained understanding of the underlying mechanisms has yet to emerge. This is a fundamental requirement to accelerate the translational identification of biomarkers and development of biologically-informed treatments.

Objectives: We surveyed a range of resting state fMRI measures capturing distinct signal properties for a comprehensive view of the functional connectome in ASD.

Methods: We examined 763 resting state functional MRI (R-fMRI) datasets (n=360 from individuals with ASD and n=403 from typical controls) available in the ABIDE repository, using several different analysis approaches. Specifically, 1) to examine local intrinsic functional connectivity (iFC) we computed *Regional Homogeneity (ReHo)*; 2) to assess local information processing we employed *Degree Centrality (DC)* a graph-based measure of network organization; 3) to capture interhemispheric connectivity we calculated *Voxel-Mirrored Homotopic Connectivity (VMHC).* Finally, beyond connectivity, we examined the *fractional amplitude of slow frequency fluctuations*(fALFF) in the BOLD signal that underlies iFC.

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Conclusions: This initial work conducted in a large sample provides a framework for investigations that take account of the regional as well as functional variation of connectivity properties in autism and can inform the dysconnection model of autism. The findings show that the use of diverse analytic approaches in R-fMRI can provide complementary evidence and a comprehensive picture of atypical functional connectivity in ASD, with some regional convergence that may direct the search for connectivity-based biomarkers.

**143.004** Linking triadic autism symptoms to distinct features of functional brain connectivity. V. Menon*, *Stanford University*

Background: An understanding of how the brain produces cognition ultimately depends on knowledge of its large-scale organization and wiring. The human brain undergoes protracted structural and functional changes during which it constructs dedicated large-scale brain networks comprised of discrete, interconnected, brain regions. Aberrations in brain connectivity have been widely reported in autism spectrum disorders (ASD), but their relation to its three core symptoms – social communication, language and repetitive-restricted behaviors are unknown.

Objectives: To examine connectivity of large-scale brain networks and to determine whether specific networks can distinguish children with ASD from typically developing (TD) children and predict symptom severity in children with ASD.

Methods: Intrinsic functional connectivity of large-scale brain networks, machine learning based classifiers built to discriminate children with ASD from TD children based on specific brain networks, and relations between brain connectivity and core symptoms of ASD.

Results: First, across three different cohorts of children, between the ages of 7 and 12, and over 100 subjects obtained from the open-source

Autism Brain Imaging Data Exchange (ABIDE) database, we found evidence for hyper-connectivity at the whole-brain level. There were significantly more links that showed hyper-connectivity than hypo-connectivity in ASD, and the degree of hyper-connectivity predicted severity of social deficits. Second, we also observed stronger functional connectivity within several large-scale brain networks in children with ASD compared with TD children. Hyper-connectivity in ASD was most prominently observed in the salience, default mode, fronto-temporal, motor, and visual networks. This hyper-connectivity result was replicated in an independent cohort obtained from ABIDE. Using maps of each individual's salience network, children with ASD could be discriminated from TD children with a classification accuracy of 78%, with 75% sensitivity and 80% specificity. The salience network showed the highest classification accuracy among all networks examined, and signals in this network predicted restricted and repetitive behavior scores. The classifier discriminated ASD from TD in the independent sample with 83% accuracy, 67% sensitivity, and 100% specificity. Third, examination of the voice-selective cortex in children with ASD revealed a striking pattern of under-connectivity between left-hemisphere posterior temporal sulcus and distributed nodes of the dopaminergic reward pathway, including bilateral ventral tegmental areas and nucleus accumbens, left-hemisphere insula, orbitofrontal cortex, and ventromedial prefrontal cortex. Furthermore, the degree of under-connectivity between voice-selective cortex and reward pathways predicted symptom severity for language communication deficits in children with ASD.

Conclusions: The three core deficits in children with ASD can be linked to distinct features of atypical functional brain connectivity in the disorder. Although under-connectivity has been posited to be a hallmark of atypical brain organization in autism, emerging findings in children with ASD are painting a decidedly more complex picture, one that has thrown into sharp relief the challenges facing our understanding of brain connectivity in autism. At the same time, they open new possibilities for a deeper understanding of the neurobiological origins of disorder.

## 144 Getting SMART about Combating Autism with Adaptive Interventions: Novel Treatment and Research Methods for Individualizing Treatment

*Discussant:* A. Pickles *King's College London*

*Organizer:* D. Almirall *University of Michigan*

The effective treatment of a wide variety of autism spectrum disorders (ASD) often requires an individualized (personalized), sequential approach to treatment, whereby treatment is dynamically adapted over time based on the individual's changing course. Adaptive interventions operationalize this type of individualized, sequential, decision making via a set of decision rules that specify whether, how, for whom, or when to alter the dosage, type or delivery of behavioral or pharmacological strategies in the treatment of autism. Adaptive interventions can be used as a guide for clinical practice. Recently, sequential multiple assignment randomized trials (SMART), a type of study design, were developed explicitly for the purpose of developing and optimizing adaptive interventions. However, adaptive interventions and SMART are new to autism researchers. The overarching aim of this methodology-oriented educational panel is to (a) provide an introduction on the application of adaptive interventions and SMART in autism treatment and research, respectively, and (b) encourage a discussion on how adaptive interventions and SMART can be used to address complex ASDs for which there is wide treatment effect heterogeneity, or for which there is an array of effective treatments, some of which may be costly or burdensome.

**144.001** Introduction to Sequential Multiple Assignment Randomized Trials (SMART) for the Development of Adaptive Interventions: Two Case Studies in Autism. D. Almirall* and S. A. Murphy, *University of Michigan*

Background: An adaptive intervention is a sequence of individually-tailored treatment decision rules that can help guide behavioral or pharmacological strategies, or their combination, for improving outcomes in the treatment of autism. Adaptive interventions realize this goal by flexibly tailoring treatments to individuals with autism when they need it most and in the most appropriate dose, thereby reducing inappropriate variance in treatment delivery and increasing the total number of individuals who benefit from treatment. Once developed, adaptive interventions can be used as treatment guidelines in public health or clinical practice. The sequential multiple assignment randomized trial (SMART), a new type of research or study design, permits researchers to collect high-quality, experimental

data that can be used to develop an optimal adaptive intervention. SMARTs realize this goal by evaluating what are the best treatment components and tailoring variables that lead to an optimal adaptive intervention.

Objectives:

In recent years, there has been a surge of interest in a variety of scientific disciplines in developing and evaluating adaptive interventions, specifically, using the SMART study design. This includes two SMART studies aimed at improving social communication in children with autism. However, despite this overwhelming interest, adaptive interventions and SMART are still new to many autism researchers. The objective of this talk is to fill this education gap concerning adaptive interventions and SMART and to encourage new ideas in the science of adaptive interventions in autism.

Methods:

We will introduce adaptive interventions and discuss why they are important. We will also introduce the SMART study design, and briefly discuss SMART study design principles, including common choices for primary and secondary aims, and allay concerns that SMART designs necessarily require prohibitively large sample sizes. These ideas will be illustrated using two SMART case-studies in autism. Both SMARTs were designed to develop and evaluate adaptive interventions for improving spoken communication in children with autism who are minimally verbal.

Results:

Adaptive interventions provide a framework to guide the individualization (personalization) of treatment for individuals with autism. SMARTs can be used to examine critical questions in the treatment of autism, such as, "Among children with autism who are minimally verbal, is it best to begin behavioral treatment with discrete trials training (DTT) or with joint-attention social play (JASP)?"; "Among children who do not respond successfully to 12 weeks of behavioral treatment, what is the effect of a treatment that combines DTT and JASP principles (DTT+JASP)?"; and "Who are the types of children more likely to benefit from combined DTT+JASP versus continuing longer with either DTT or JASP?".

Conclusions:

Adaptive interventions have great potential for improving outcomes in individuals with autism, by capitalizing on individual heterogeneity in response to treatment. However, the science of adaptive interventions is still in its infancy in autism. SMART studies have the potential to improve our scientific understanding of how to develop the best possible adaptive intervention.

**144.002** SMART Approach to Increasing Communication Outcomes in ASD. A. P. Kaiser*[1] and .. CCNIA and AIM ASD Research Networks[2], (1)*Vanderbilt University*, (2)*University of California, Los Angeles; Vanderbilt University, Nashville, TN; Kennedy Krieger Institute, Baltimore, MD; University of Rochester, NY; Cornell University, New York, NY; University of Michigan*

Background: Social-communication impairment is a significant issue for children with autism spectrum disorders (ASD). While most children learn to communicate with spoken language, approximately 25-30% of children with ASD remain minimally verbal, even after years of intervention. Failure to develop spoken language by age 5 years increases the likelihood of a poor long-term prognosis for social and adaptive functioning. Due to the great heterogeneity in abilities of minimally verbal children with ASD, a sequential adaptive treatment design offers potential for improving outcomes in children who have been slow responders to early language based interventions.

Objectives: This study blended two evidence based social communication interventions for language impaired children, JASPER and Enhanced Milieu Teaching and tested the effect of beginning treatment with a speech-generating device in the context of an adaptive treatment design for improving spontaneous, communicative utterances in school- aged, minimally verbal children with autism.

Methods: Sixty-one minimally verbal children with autism, aged 5 to 8 years were randomized to the blended developmental/behavioral intervention (JASP + EMT) with or without the augmentation of a speech-generating device (SGD) for 6 months with a 3- month follow up. The intervention consisted of two stages. In Stage 1 all children received two sessions per

week for 3 months. Stage 2 intervention was adapted (increased sessions or adding the SGD) based on the child's early response. The primary outcome was the total number of spontaneous communicative utterances; secondary measures were total number of novel words, total comments from a natural language sample.

Results: Primary aim results found improvements in spontaneous communicative utterances, novel words, and comments all favored the blended behavioral intervention that began by including an SGD (JASP+EMT+SGD) as opposed to spoken words alone (JASP+EMT). Secondary aim results suggest that the adaptive intervention beginning with JASP+EMT+SGD and intensifying JASP+EMT+SGD for children who were slow responders led to better post-treatment outcomes.

Conclusions: Minimally verbal school aged children can make significant and rapid gains in spoken spontaneous language with a novel blended intervention that focuses on joint engagement and play skills and incorporates an SGD. A new research project, AIM-ASD, is focused on further tailoring of intervention components by also including parent training and other methods of communication interventions.

**144.003** Modularized evidence-based clinical decision-making: A rescue protocol for non-responders. C. Kasari*[1] and B. F. Chorpita[2], (1)*University of California Los Angeles*, (2)*University of California, Los Angeles*

Background: A vexing issue in treating children with ASD is that there is great heterogeneity in presentation and in response to evidence based treatments (EBTs). Recognition of this heterogeneity in many areas of mental health, along with the realization that EBTs for different conditions have a variety of core principles in common, has led researchers to consider a modularized approach to the application of EBTs. In this approach, modules (or specific behavioral strategies) from one treatment manual may be flexibly applied with those of another treatment manual to address the complex, and possibly heterogeneous, needs of the child. Since the decisions to apply different modules may unfold over time (e.g., across different treatment sessions) as more is learned about the child's complex needs or as needs change, this modularized approach can be seen as a form of adaptive intervention. However, this treatment approach has not been studied in children with autism. In children with ASD who are minimally verbal, this type of modularized, adaptive approach may be especially useful as a "rescue protocol" for children who have been identified as non- or slow-responders to a previous trial of a manualized EBT, such as discrete trials training (DTT) or joint-attention social play (JASP) intervention.

Objectives: The overarching objective of this presentation is to present pilot data on the application of this adaptive, modularized approach among children identified as non-responders or slow-responders to a 6 week trial of DTT or JASP. Specifically, we will present data on the usefulness of implementing a "treatment dashboard" used to organize the choices of modules in a novel, blended DTT+JASP treatment approach for these non- or slow-responding children. We refer to the blended DTT+JASP intervention as a "rescue protocol", defined as combinations of modules and strategies from both DTT and JASP.

Methods: Case-studies are drawn from a SMART design in which (i) minimally verbal children with ASD are randomized initially to one of two EBTs (DTT or JASP), and (ii) after 6 weeks, non- or slow-responders to initial DTT or JASP are randomized to continue on their initial treatment for an additional 6 weeks or to the rescue protocol (blended DTT+JASP).

Results: We will present data from illustrative case-studies of the treatment dashboard including (i) the assessments, treatment history, and child responses used by clinicians to select from a systematic menu of DTT+JASP modules in the dashboard, (ii) the rules used to make these decisions, and (iii) the benefits, challenges and obstacles to implementing such an approach, including acceptability and feasibility issues.

Conclusions: Minimally verbal school aged children have potential for making significant gains in spoken spontaneous language using current EBTs. However, some will continue to make slow progress, and may benefit from combinations of treatment plans that are systematically implemented based on the child's treatment history and progress in treatment. A modularized, adaptive intervention approach using new behavioral health reporting systems

can assist clinicians and researchers in personalizing the implementation of significant components of these EBTs.

**144.004** Adaptive Intervention for Peer-Related Social Skills for Children with Autism Spectrum Disorders: Identifying Patterns Indicating Need for Change in Treatment. W. Shih*[1] and S. Patterson[2], (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

Background: Social challenges are a significant concern for children with Autism Spectrum Disorder (ASD) across a wide range of abilities and ages. These challenges may be most evident at school where mainstreamed children with ASD report significant difficulty in developing positive peer relationships. For example, some children appear to be unaware of their peers on the yard, while others attempt to play and join in but their social initiations may be awkward or ineffective. Still others are popular with their peers. This wide variation in the social characteristics of children with ASD suggests that there are likely different intervention needs. Adapting interventions based on children's response to intervention is a necessary next step that is currently limited in the autism research literature.

Objectives: The purpose of this study was to explore methods for understanding the trajectories of children's response to treatment prior to end of treatment in order to inform adaptive treatment models for future studies.

Methods: Participants with ASD were drawn from a randomized controlled trial comparing two different social skills interventions at children's schools. We explored whether playground engagement scores measured at entry and midpoint of treatment predicted their engagement scores at exit using the Classification and Regression Tree (CART) method. The CART method defines splits in the data that can then help professionals make data-based decisions about the individualization and adaptation of evidence-based social skills interventions.

Results: Using the CART approach, four meaningful subgroups based on children's playground engagement scores measured at entry and changes from entry to midpoint were identified using three splits. All the splits were determined recursively by the CART algorithm. The first split was based on how much the children's percent time engaged changed from entry to midpoint by at least 14.01% from entry to midpoint. Among those who did not increase at least 14.01% from entry to midpoint, a second split was conducted. The second split was based on whether the children's total percent time engaged with peers was greater than 51% at entry and this split separated theses children into two subgroups. Lastly, among those who did increase from 14.01% from entry to midpoint, again a third split was applied. For this group, the third split was based on whether the children's total percent time engaged with peers was greater than 19.38% at entry and separated them into another two subgroups.

Conclusions: This study illustrates the substantial heterogeneity in children's response to treatment with multiple clinically salient subgroups embedded within the larger group. The data suggest that measurements of children's behavior mid-study can be used to predict children's treatment outcomes. Such data may be used to inform decisions to augment or alter programming prior to treatment exit in order to tailor intervention to best meet the needs of individual children and the CART method can be useful in defining metrics that could be used to build an adaptive treatment sequences for children.

## 145 Resilience in Infants at High Risk for Developing Autism Spectrum Disorders

*Discussant:* L. J. Carver *University of California, San Diego*

*Organizer:* L. J. Carver *University of California, San Diego*

Infant siblings of children with autism spectrum disorders are at increased risk for developing the disorder, and, even when unaffected, often show early signs consistent with ASD symptoms. Tracking early development in infant siblings of children with ASD can help with identifying early precursors to the development of ASD. Researchers who have been following children with ASD have noted that some children who show early signs associated with ASD later show patterns more consistent with typical development. An important, but often overlooked research question is what factors protect infants at risk from developing ASD. The talks in the proposed symposium describe studies of children who show trajectories of development that are consistent with resilient development. The presentations using converging methods including eye tracking and behavioral assessments to show patterns of improving trajectory and lessening symptoms in a subset of children who show early characteristics of ASD. Presentations

will also discuss possible mechanisms for resilience, including early infant-caregiver interactions and looking behavior. We will also discuss implications of resilience for developing early intervention and prevention strategies.

**145.001** Communication Development in Infant Siblings of Children with ASD: Evidence of Resiliency. C. Hess, R. Landa*, K. Boswell and J. P. Sharpless, *Kennedy Krieger Institute*

Background:

Social and communication delays are considered risk indicators for ASD in late infancy to early toddlerhood. Such delays have been identified in younger siblings of children with ASD (Landa & Garrett-Mayer, 2006). Yet recent findings indicate that early language delays are transient in some younger siblings of children with ASD (Landa, Gross, Stuart & Bauman, 2012).

Objectives:

Examine stability of social and language delays from late infancy through the period of expected first word acquisition.

Methods:

Participants are from an ongoing longitudinal study of younger siblings of children with autism (HR infants) and children at low risk for ASD (LR; no family history of autism). Data are presented from testing completed at ages 10 (22 LR; 50 HR) and 14 months (14 LR; 30 HR) (sample size will be larger by IMFAR). Frequency of initiation of joint attention (IJA) and behavior regulatory (IBR) bids as well as inventory of communicative gestures and communicative consonants were measured using the Communication and Symbolic Behavior Scales Developmental Profile (CSBS DP; Wetherby & Prizant, 2002). Repeated measures ANOVA was used for group comparisons; post hoc analyses were conducted.

Results:

Significant between-group differences were found at age 10 months. Post hocs revealed that the HR group performed significantly lower than the LR group on all four dependent variables (*p*s from .02 to <.001). Longitudinal analyses revealed significant effects for Time ($p$ = .04) and Time x Group (p=.004) for IJA, and a significant effect for Time (p<.001) for IBR. At age 14 months, the LR and HR groups produced IJA bids with similar frequency, but the LR group produced significantly fewer IBR. From 10 to 14 months of age, the LR group's frequency of IJA remained stable, but the HR group showed a rapid and robust increase in frequency of IJA. The slope of the gain in frequency of initiation of IBR in the HR and LR groups was similar and parallel, but the HR group did not 'catch up' to the LR group in rate of producing such communicative bids.

Conclusions:

Findings reveal global delay in the prelinguistic phase of expressive communication development in HR siblings at age 10 months, with lingering delay in isolated aspects of communication at 14 months. The late-infancy communication delay in HR siblings is characterized by decreased overall level of producing communicative bids, whether social (IJA) or non-social (IBR) in nature, as well as by a restricted repertoire of communicative forms. This means that the communicative bids of HR siblings are poorly differentiated and that these children are not initiating communicative engagement with others at expected rates during late infancy. These findings have implications for resiliency in some aspects of development within HR siblings, who 'catch up' to LR age peers by 14 months, although they continue to show delay in frequency of behavior regulatory bids.

**145.002** A first glimpse of the developmental profile of sibling resilience: 2-24 months eye tracking-based developmental trajectories of eye fixation. W. Jones[1] and A. Klin*[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*

Background: We recently created eye tracking-based "growth charts" of social visual engagement via Functional Data Analysis of data collected at 2-24 months (10 data points) for N=32 infants ascertained diagnostically at age 36 months as either having ASD (N=13) or typical development (TD; N=29). From the 2nd month onwards (to 24 months), infants later diagnosed with ASD exhibit mean decline in eye fixation relative to TD infants; this decline is highly correlated with severity of clinical outcome at 24 months ($r$= -0.75, $p$ = 0.007); and decline in the first year alone predicts severity of future outcome ($r$= -0.71, $p$= 0.015).

Objectives: We hypothesized that A. this decline mirrors failure in transition from experience-expectant, reflexive, sub-cortically guided eye

fixation to experience-dependent, interactive, cortically guided eye fixation; and B. early divergence from normative development suggests a means by which diverse genetic liabilities are instantiated into a spectrum of affectedness.

Methods: To explore the latter, we used this dimensional assay (decline in eye fixation) to guide the analyses of developmental trajectories of siblings who were ascertained at 36 months as either unaffected (HR-ASD_No-Dx; N=18) or infants with transient/subthreshold ASD symptoms, or BAP (HR-ASD_BAP; N=10). We divided this group on the basis of early decline in eye fixation.

Results: 16 infants exhibited no sign of early decline – 15 were clinically unaffected at outcome (HR-ASD_No-Dx), while 1 was identified as BAP (HR-ASD_BAP). These infants exhibit remarkably similar developmental change in eye fixation, across all growth measures quantifying this process. In contrast, 12 showed signs of early decline in eye fixation – 9 were identified at outcome as BAP and 3 as unaffected. In these infants, although their eye fixation is initially in decline, it changes course and begins to increase at approximately 18 months of age. More remarkably, we see in the 2$^{nd}$derivative that the developmental changes leading to the 18-month course correction actually have their origins at approximately 9 months of age, when the developmental decline reaches a point of inflection.

Conclusions: This contrast, between the developmental trajectory for infants who later met criteria for ASD versus the trajectory for those who showed early eye fixation decline but did not ultimately receive a diagnosis, may offer a first glimpse of the developmental profile of sibling resilience. We hypothesize that "rate of change" (the 2$^{nd}$ derivative) most closely reflects activity (onset/change/completion) of underlying biological processes, and may constitute a quantitative behavioral phenotype delimiting a window of opportunity (around 9 months) for intervention that could capitalize on potential for resilience, which is expressed naturally in some siblings but not in others.

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**145.003** "Optimal early social environment" as a protective factor for at-risk infants? A closer study of parent-infant interactions. M. W. Wan* and J. Green, *University of Manchester*

Background: We recently reported from the British Autism Study of Infant Siblings (BASIS) that 6- and 12-month parent-infant interactions in at-risk siblings differ from those with low-risk, and that – among at-risk siblings – particular global aspects of interaction at 12 months predicted 3-year classification of autism spectrum disorder (ASD) (Wan et al., 2013). This supports recent models of the early emergence of ASD in which infant intrinsic risk susceptibilities in behaviour may be amplified by interaction within the early social environment into an increasingly atypical developmental trajectory. Conversely, it follows that optimising the early social environment of infants at risk of ASD may serve as a protective or 'resiliency' factor.

Objectives: To examine in a series of exploratory analyses whether those at-risk infants (of siblings with ASD) with early behavioural atypicalities but more optimal parent-infant interactions at 12 months were less likely to receive an ASD diagnosis outcome at 3 years than those with lower quality interactions.

Methods: Six-min videotaped episodes of parent-infant unstructured play of infants at 6-10 months and 12-15 months in at-risk and low-risk infants in a laboratory setting were rated blind on the *Manchester Assessment of Caregiver-Infant Interaction* (MACI). The *Autism Observation Scale for Infants*(AOSI) was administered for concurrent behavioural signs of ASD features. Systematic consensus diagnostic classification of ASD was made at 3 years for the at-risk siblings.

Results: Within our cohort of infants at familial risk of ASD (N = 43), we identified a sub-group with elevated behavioural atypicalties at 12 months (AOSI total score >3; n = 20). In this high-atypicality group, 50% whose parent-infant interactions were rated as low in mutuality received an ASD classification at 3 years compared with 17% of those with mutual interactions (and none of the low-atypicality high-mutuality group received an ASD diagnosis). Although we had previously reported group differences by at-risk status (at-risk ASD, at-risk no-ASD, low risk) in parent interactive behaviours at 6 and 12 months, among the high-atypicality group, it was MACI infant affect that most

differentiated those who went onto receive a diagnosis (67% with more positive affect compared with 18% with more negative affect). However, this may reflect infant positivity *within the parent-infant interactive context* rather than infant social skill, since 60% of infants who showed a social smile (response to examiner) in the AOSI were rated as showing positive affect in parent-infant interaction, and AOSI social smile alone did not predict later diagnosis. Exploratory analyses of other areas of parent-infant interaction will also be presented.

Conclusions: The possibilities for building resilience in this at-risk group (or not) will be discussed based on these sub-group analyses and our previous findings from the complete sample. There are insights and limitations in studying whether the early interactive context may serve as a protective factor for infants at very high risk (familial risk and behaviourally) of ASD. Finally, we will consider the implications for early social interventions which focus on optimising parent-infant interaction in infants with an older sibling with ASD.

**145.004** Early Characteristics of Children Who Lose Their Autism Diagnosis Between Age 2 and 4. E. Moulton*[1], D. A. Fein[1], M. L. Barton[1] and D. Robins[2], (1)*University of Connecticut*, (2)*Georgia State University*

Background:

Emerging literature has indicated that a subset of children with a documented ASD lose their diagnosis and function in the average range of cognition and behavior. Multiple factors including intervention, symptom severity, adaptive functioning, motor skills and language abilities may help to predict positive outcomes. Prospective research will help to increase our understanding of the rate of optimal outcomes and the early characteristics of children who attain them.

Objectives:

To explore child-level factors at age two that differentiate children who attain an optimal outcome from those who retain their ASD diagnosis at age four in a prospective study.

Methods:

214 children were diagnosed with an ASD, by clinical best estimate, at an average age of 26 months (Time- 1) following positive screening on an autism-specific screener (M-CHAT(-R)). The Autism Diagnostic Observation Schedule (ADOS), Mullen Scales of Early Learning, Vineland Adaptive Behavior Scales (VABS-II), and Childhood Autism Rating Scale (CARS) were completed.

At an average age of 53 months (Time-2), children were re-evaluated; 171 (80%) children retained an ASD diagnosis (ASD-ASD). Of these, 33 have older or same-aged siblings on the spectrum. 19 children (9%) were determined to meet the following criteria for an "optimal outcome"(OO): no longer met criteria for any ASD, and functioning in the average range (within 1.5 SD of the mean) on standardized measures of cognition, language, social and communication skills. Of these 19 children, 3 have older or same-aged siblings on the spectrum. 24 children moved to a different diagnosis (e.g., Global Delay) and will not be considered further here.

Results:

A Chi-square test for independence indicated that children initially diagnosed with PDD-NOS were more likely to attain an optimal outcome (13.8%) than children initially diagnosed with AD (7.0%)($p$=.046). Independent groups t-tests compared ADOS, Mullen, VABS-II, CARS and DSM-IV symptoms of the OO group (N=19) to the ASD-ASD group (N=171) at Time-1. No significant group differences were found in Time-1 ADOS scores, providing evidence against simple misdiagnosis at age two. For DSM-IV symptoms, the OO group had fewer restricted/repetitive behaviors (RRBs) than the ASD-ASD group ($p$=.01). In addition, the OO group had less severe autism as measured by the CARS ($M$=28.7 vs. $M$=33.02, $p$=.001). The OO group was higher on Daily Living ($p$=.03) and Motor Skills ($p$=.01) on the VABS-II. No significant group differences were found in the areas of cognitive or language skills.

Conclusions:

Nine percent of children diagnosed with an ASD attained optimal outcome by age four. At age two, these children showed fewer RRBs, lower symptom severity, more diagnoses of PDD-NOS as opposed to Autistic Disorder, and higher daily

living and motor skills than those who retained their diagnosis. RRBs have been found in other studies to be a negative prognostic factor, and may reflect the fact that these children are less attentive to intervention and natural social interactions. Early motor skills have also previously been found to predict outcome and may function as a better indication of CNS integrity than social or language skills in children with impaired motivation to interact.

## 146 Phenomenology and Impact of Internalizing Symptoms in ASD Across the Lifespan

*Discussant:* S. W. White *Virginia Polytechnic Institute and State University*

*Organizer:* K. Gotham *Vanderbilt University*

Internalizing comorbidity in the ASD population has received increasing attention due to its observed prevalence and clinical reports of associated impairment, however its exact relation to and impact within ASD are unclear. In this panel, we elucidate the phenomenology of anxiety and depressive symptoms in ASD using well-characterized samples spanning early school-age to mid-adulthood. Data on internalizing comorbidity patterns will be presented from a developmental perspective, and with particular emphasis on disentangling whether these symptoms are consistent with the ASD phenotype versus separable and additive. Measurement of comorbid internalizing symptoms is considered across raters and using novel methodology (e.g., eye-tracking). Finally, we will present cutting-edge findings on the impact and outcome of affective distress in ASD from a variety of perspectives. We take a transdiagnostic approach to both internalizing symptoms (focusing on emotional distress and symptom ratings rather than categorical disorders), and to their potential mechanisms (e.g., gaze patterns and emotion regulation ratings are compared across ASD and typical controls). Discussion will focus on methodological considerations associated with psychiatric comorbidity patterns in ASD, and specifically on designing clinical research that is sensitive to transdiagnostic issues and employs state-of-the-art and novel measurement of internalizing symptoms across the lifespan.

**146.001** Modeling Growth of Internalizing Symptoms from Childhood through Young Adulthood in Autism Spectrum and Developmentally Delayed Samples. K. Gotham*[1], S. M. Brunwasser[1] and C. Lord[2], (1)*Vanderbilt University*, (2)*Weill Cornell Medical College*

**Background:** Previous reports of longitudinal patterns in internalizing symptoms within autism spectrum disorders (ASD) have focused on narrow childhood age ranges or used dependent variables not specific to affect or anxiety (e.g., Hallett et al., 2010; Taylor & Mailick, 2010). We modeled longitudinal change in individuals with ASD and developmentally delayed (DD) controls using subscales from a widely-used, well-validated measure of internalizing behavior, the Child Behavior Checklist 6-18 (CBCL; Achenbach & Rescorla, 2001).

**Objectives:** To (1) model growth in anxiety and depressive symptoms from late schoolage through young adulthood in a DD sample; (2) to evaluate differences in developmental patterns of internalizing symptoms based on diagnostic status (ASD versus nonspectrum) and verbal IQ (VIQ); (3) to assess relationships between internalizing growth patterns, baseline predictors (e.g., executive functioning, externalizing behaviors), and distal outcomes (e.g., functional independence, quality of life ratings), controlling for VIQ and autism severity.

**Methods:** Our sample included 158 participants (n=105 with ASD; n=53 with heterogeneous nonspectrum disorders or early DD) who had between 2 and 7 repeat iterations of the parent-rated CBCL. *ASD*: age ranged from 6-23 years (M=16 years; SD=4 years); *Nonspectrum*: 7-24 years (M=17; SD=3). *ASD*: VIQ ranged from 11-141 (M=62; SD=41); *Nonspectrum* from 10-139 (M=83; SD=31). As consecutive clinic referrals at age 2, most participants received full diagnostic evaluations around ages 2, 3, 5, 9, and 18-22 years, and families completed parent- and self-report questionnaires at regular intervals of 3–6 months between ages 9 and 24. CBCL Anxious-Depressed, Anxiety, and Affective subscale distributions were positively skewed, so outcomes were treated as count variables; we used mixed-effects Poisson models with a logarithmic function rather than traditional growth models which assume normally distributed residuals. All models contained random intercept and slope terms to capture between-person variability in initial symptom levels and rate of growth over time, with fixed effects of diagnosis, mean-centered age and VIQ, and diagnosis-age interaction.

**Results:** We observed an interaction between age and diagnosis for the Anxious-Depressed aggregate scale (b=0.005, 95% CI [0.002, 0.008]), with significant increases in symptoms over time in the ASD group alone (b=0.004, 95% CI [0.001, 0.006]). ASD was associated with

higher Anxiety (b=0.491, 95% CI [0.068, 0.913]) and Affective (b=0.547, 95% CI [0.138, 0.957]) scores overall. Anxiety subscale scores increased significantly with age in both diagnostic groups, with no difference in rate of change over time (b=-.004, 95% CI [-0.012, 0.003]). Affective subscale scores did not change significantly over time in either group (b=-0.006, 95% CI [-0.015, 0.003]). Higher VIQ was associated with higher levels of Anxious-Depressed (b=0.012, 95% CI [0.008, 0.016]) and Anxiety symptoms (b=0.006, 95% CI [0.002, 0.009]); VIQ was not associated with Affective scores (b=-0.002, 95% CI [-0.003, 0.006]).

**Conclusions**: These preliminary findings support previous claims that individuals with ASD are at particular risk for affect- and anxiety-specific internalizing problems, and provide initial empirical support for the notion of anxiety symptoms increasing into adulthood within ASD. Findings on baseline predictors, including emotion regulation scores, and distal outcomes related to internalizing symptoms also will be presented.

**146.002** Is it Anxiety and Does it Matter? Exploring the Manifestations and Costs of Anxiety and Other Symptoms of Distress in Youth with ASD.

C. M. Kerns*[1], M. D. Lerner[2], S. W. White[3], P. C. Kendall[4], J. Herrington[5], J. Miller[6], M. Franklin[5], T. H. Ollendick[7], J. J. Wood[8], G. Ginsburg[9], B. McLeod[10], S. Compton[11] and J. Piacentini[8], (1)*Drexel University*, (2)*Stony Brook University*, (3)*Virginia Polytechnic Institute and State University*, (4)*Temple University*, (5)*University of Pennsylvania*, (6)*Center for Autism Research, Children's Hospital of Philadelphia*, (7)*Virginia Polytechnic University*, (8)*University of California Los Angeles*, (9)*John Hopkins Medical Institute*, (10)*Virginia Commonwealth University*, (11)*Duke University*

**Background:** Despite growing study and treatment, questions remain about presentation, measurement and impact of anxiety in ASD. Do symptoms of anxiety in ASD resemble traditional anxiety disorder symptoms? Do they incur similar costs? Few studies have directly addressed these crucial issues, which underscore the importance of this research. Limitations of prior studies include lack of (a) well-characterized ASD samples and (b) methods for differentiating anxiety and ASD symptoms or quantifying dissimilarities in anxiety presentation across youth with and without ASD.

**Objectives:** This project (1) examines the degree to which the underlying construct of self- and parent-reported anxiety is consistent across putatively anxious children with and without ASD, and (2) assesses challenges independently associated with DSM-consistent and -inconsistent manifestations of anxiety in well-characterized samples of youth.

**Methods:** *Study 1* employs Multigroup Factorial Invariance (MFI) analyses using Structural Equation Modeling to examine degree of construct equivalence of anxiety on the Multidimensional Anxiety Scale for Children (parent and child reports). The sample includes children with anxiety disorders and ASD with intact verbal ability (n = 109, $M_{age}$ = 11.67 years) and a matched comparison group with anxiety disorders, but not ASD (n = 342, $M_{age}$ = 11.25 years). *Study* 2 examines associations between parent reports of behavior, social assertiveness and parent stress with impairing levels of DSM-consistent and inconsistent anxiety, which were differentiated via a parent/child semi-structured diagnostic interview in 59 participants (7–17 years, $M_{age}$= 10.56 years; IQ range: 47-158) with ASD.

**Results:** *Study 1*. MFI analyses indicated similar factors (i.e., physical avoidance, harm avoidance, social anxiety, separation/panic) in children with ASD using the MASC-C, but not the MASC-P. Dissimilar factors were found for the MASC-P (i.e. metric invariance was not supported): Exploratory Factor Analysis in the ASD group indicated four novel MASC-P factors: a subset of separation/panic, *low* social anxiety, physical, and performance anxiety symptoms. *Study 2.* DSM-consistent anxiety disorders were associated with more self-injurious behavior and depression in youth with ASD, but also better functional communication, after controlling for other influential variables (e.g. ASD severity, IQ, DSM-inconsistent anxiety). By comparison, DSM-inconsistent anxiety was associated with increased parental stress, after controlling for correlation with other variables (e.g. ASD severity, DSM-consistent anxiety disorders). Neither DSM-consistent nor inconsistent anxiety was associated with social assertiveness.

**Conclusions**: Similarities in the latent factor structure of child, but not parent, reports on the MASC add to the notion that youth with ASD may manifest anxiety and distress in ways both similar and dissimilar to typically-developing youth. Findings from Study 2 support a specific profile of challenges and relative strengths associated with

distinct manifestations of anxiety in ASD. Whereas traditional anxiety disorders were uniquely associated with more self-injurious behavior and depression, parent stress was associated with DSM-inconsistent symptoms. Results provide a strong rationale for efforts to better understand and measure anxiety as it presents in ASD. Whether the dissimilar presentations elucidated in these studies reflect variants of anxiety disorder, general distress or symptoms of ASD will be considered, and implications for treatment and future research discussed.

**146.003** Emotion Regulation Patterns in Adolescents with High-Functioning Autism Spectrum Disorder: Comparison to Typically-Developing Adolescents and Association with Psychiatric Symptoms. C. A. Mazefsky*[1], X. Borue[1], T. N. Day[2] and N. J. Minshew[1], (1)*University of Pittsburgh School of Medicine*, (2)*University of Pittsburgh*

**Background:** Autism spectrum disorder (ASD) is often associated with poor emotional control and psychopathology, such as anxiety and depression. However, little is known about the underlying mechanisms. Emotion regulation (ER) is a potential contributing factor, but there has been limited research on ER and its role in comorbid psychopathology in ASD. We know especially little about the rate at which individuals with ASD engage in involuntary ER responses as the few existing studies have focused on effortful control strategies (e.g. cognitive re-appraisal).

**Objectives:** This study aimed to: 1) Explore patterns of both voluntary and involuntary forms of ER in adolescents with high-functioning ASD; 2) Investigate how ER corresponds to manifestations of psychopathology.

**Methods:** Participants included 25 high-functioning adolescents with ASD and 23 age- and IQ-matched typically-developing (TD) controls. Participants completed the Response to Stress Questionnaire, Social Stress Version (RSQs) as a measure of voluntary and involuntary ER processes. Parent- and self-reports of psychopathology were obtained, including broad measures of internalizing and externalizing problems and specific assessments of anxiety and depression.

**Results:** Contrary to expectations, both groups reported similar levels of adaptive, effortful control forms of ER (re-appraisal, problem-solving, acceptance, etc.). However, the ASD group reported significantly greater use of involuntary forms of ER that are typically maladaptive, including involuntary engagement (rumination, intrusive thoughts, emotional arousal, and involuntary action) and involuntary disengagement (emotional numbing, cognitive interference, inaction, and escape). Associations between ER and psychopathology were generally more robust using self- rather than parent-report. For both groups, greater endorsement of involuntary ER strategies was associated with higher ratings of psychopathology, whereas the use of effortful control approaches was significantly associated with lower levels of psychopathology. The magnitude and direction of association between ER types and psychopathology were similar for measures of depression and anxiety.

**Conclusions:** This was the first study to examine ER in adolescents with ASD. Our finding that the ASD and TD groups did not differ in their use of effortful ER (primary and secondary control) differs from prior studies with children [Rieffe et al., 2011] and adults [Samson et al., 2012]. Longitudinal follow-up studies are warranted to clarify whether adolescence is an ideal window for ER-related prevention and treatment efforts in ASD. The ASD group did report significantly higher rates of involuntary ER approaches that are usually considered maladaptive. This finding lends some support to the previously untested contention that ER in ASD may be characterized by more internally-driven responses that are less organized and goal-directed than in non-ASD populations [Mazefsky et al., 2013]. Further, greater use of involuntary forms of ER was related to higher levels on broad measures of internalizing and externalizing behaviors as well as specific assessments of anxiety and depressive symptoms. These findings can help guide the development of psychosocial treatments targeting dysfunctional ER in adolescents with ASD. Given that patterns of association were fairly similar for both anxiety and depression, a transdiagnostic approach targeting ER skills, rather than discrete disorders, may prove useful across the different manifestations of emotional distress in ASD.

**146.004** Eye-Gaze Pattern Analysis As a Key to Understanding Co-Occurring Social Anxiety within Autism Spectrum Disorder. B. B. Maddox* and S. W. White, *Virginia Polytechnic Institute and State University*

Background: Emerging research suggests that many adolescents and adults with Autism Spectrum Disorder (ASD) experience impairing social anxiety (Kreiser & White, 2013), yet there is little guidance or agreement about how to best assess social anxiety in this population. Eye-tracking methodology may prove useful in identifying and characterizing co-occurring social anxiety in adults with ASD. Social anxiety in non-ASD samples has been associated with a vigilance-avoidance gaze pattern (Garner et al., 2006), but this type of eye-tracking analysis has not been applied to individuals with ASD and co-occurring social anxiety.

Objectives: The primary objective is to explore the influence of co-occurring social anxiety on gaze patterns in individuals with ASD. We provide a developmental perspective by combining data from an adolescent sample and an adult sample.

Methods: Data are drawn from two separate eye-tracking studies, both of which used the NimStim Set of Facial Expressions (Tottenham et al., 2009). Each stimulus presentation contained a pair of photographs of the same person, with one photo depicting an emotional expression and the other depicting a neutral or different emotional expression. All participants with ASD had a confirmed diagnosis based on the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2002). In the adolescent study, a sample of 33 participants (12-17 years old; 15 with ASD) completed the eye-tracking task. The adolescents and their parents also completed measures of ASD symptom severity and social anxiety. The adult study involves a three-group design, with 25 participants (age 16-45) per group: individuals with ASD, individuals with Social Anxiety Disorder (as supported by the Anxiety Disorders Interview Schedule [ADIS]; Brown et al., 1994), and non-socially anxious individuals without ASD. All participants completed the eye-tracking task, various questionnaires, a brief cognitive assessment and clinical interview, and the ADIS social anxiety module.

Results: Preliminary analyses from the adolescent study show that greater self-reported fear of negative evaluation is associated with longer gaze duration to socially threatening cues (i.e., human faces expressing disgust) in the participants with ASD ($r = .75$, $p = .031$). This relationship between self-reported social anxiety and gaze duration toward faces displaying disgust was not seen in the group of adolescents without ASD. The ASD group, with relatively high levels of social anxiety, was also quicker to disengage attention from disgust faces, relative to the non-ASD group. Data collection is projected to be complete for the adult study by November 2013, and results from this well-characterized sample will be presented.

Conclusions: Preliminary results highlight the importance of considering co-occurring social anxiety when conducting eye-tracking research with ASD. If a vigilance-avoidance gaze pattern (similar to that seen in non-ASD individuals with social anxiety) is found in the participants with ASD and social anxiety, then eye-tracking methodology could provide support for social anxiety being a separable phenomenon in ASD. The exploration of gaze pattern data to assess psychiatric comorbidity in individuals with ASD is novel and will require more research in the future. Clinical and scientific implications related to eye-tracking and ASD will be discussed.

## 147 IGF-1 and Its Analogs: Restoration of Biological Deficits in Neurodevelopmental Disorders Associated with Autism

*Discussant:* J. Horrigan *Neuren Pharmaceuticals*

*Organizer:* O. Shcheglovitov *Stanford University School of Medicine*

Recent studies have demonstrated the effectiveness of IGF-1 and related compounds to restore biological deficits in neurodevelopmental disorders associated with autism and intellectual disability, including Rett, Fragile X, and Phelan-McDermid Syndromes. Although, these disorders are caused by different genetic abnormalities, the ameliorative effects of IGF-1 and IGF-1(1-3) suggest the presence of common rescue pathways. In this session, we bring together individuals with diverse expertise that are studying cellular, molecular and behavioral phenotypes associated with Rett, Fragile X and Phelan-McDermid Syndromes, using animal and human models. The participants discuss the relevant mechanisms of action and perspectives on using IGF1 and its analogs as novel therapeutic agents for patients with ASDs.

**147.001** IGF-1 and its Analogs: Restoration of Biological Deficits in mouse models of Fragile X and Rett Syndromes. L. Glass*[1], F. J. Altimiras[2], M. Snape[3], J. Horrigan[1] and P. Cogram[2], (1)*Neuren Pharmaceuticals*, (2)*Molecular and Clinical Pharmacology Program, Institute of Biomedical Sciencies,*

*Faculty of Medicine, University of Chile*, (3)*Autism Therapeutics Ltd*

Background: IGF-1 and its n-terminal tripeptide ([1-3]IGF-1) are widely distributed in the CNS and exert a range of effects on neurons in the normal state (Corvin et al, 2012; Ramsey et al, 2005). These neurotrophic factors also have been reported to effect synaptic function and other processes in certain pathological states including neurodevelopmental disorders (Riikonen et al, 2003; Tropea et al, 2009; Landi et al, 2011; Bozdagi et al, 2013) and brain injury (Lu et al, 2009; Rubovitch et al, 2010; Madathil et al, 2010). NNZ-2566 is a synthetic analog of (1-3)IGF-1 with longer half-life and oral availability.

Objectives: We conducted experiments to characterize the effects of NNZ-2566 in vitro and in vivo in a model of Fragile X Syndrome (*fmr1* knockout) at doses comparable to those being utilized in Phase II clinical trials of Rett Syndrome (ClinicalTrials.gov ID: NCT00299312) and Fragile X Syndrome (ClinicalTrials.gov ID: NCT01894958).

Methods: *Fmr1* KO and wild-type mice (C57BL/6J background) were dosed with either vehicle or NNZ-2566 (100 mg/kg i.p.) 1/day, starting at 14 weeks of age, for 28 days. Behavioral, anatomic and molecular effects were assessed following treatment. Western blot analysis was conducted on extracellular-signal-regulated kinase (ERK), and Akt from wild-type and fmr1 KO mouse brain (obtained ex vivo, following 28 day treatment with NNZ-2566 or vehicle). Dissociated hippocampal cells were plated in 15 mm multi-well vessels and a plating medium of MEM-Eagle's salts (glutamine free) was supplemented with 10% FBS. After 3 days (culture conditions: 37 °C in humidified 5% $CO_2$), GFP was applied to monitor dendritic spine morphogenesis during culture. Cells were treated with NNZ-2566 (50 nM).

Results: NNZ-2566 normalized differences between *fmr1* KO and wild-type mice in all behavioral outcomes assessed and normalized macro-orchidism in the *fmr1* KO mice. Dendritic spines usually form between 7 and 14 days in vitro (DIV). By 14 DIV most dendritic protrusions are spines; however, their maturation continues until 21 DIV. Fmr1 KO significantly increased spine density. Increased spine density was reversed by in vitro treatment with NNZ-2566. ERK is a MAPK signal transduction protein, responsible for growth factor transduction, proliferation and cytokine response to stress and apoptosis. Akt is a key component in the PI3K/Akt/mTOR signalling pathway and regulates cellular survival and metabolism by binding and regulating downstream effectors. Fmr1 KO exhibited increased ERK and Akt phosphorylation. This effect was reversed by NNZ-2566. Nrf2 (nuclear erythroid 2-related factor 2) is a leucine-zipper transcription factor, which binds to the antioxidant response elements (ARE) thereby regulating the expression of genes involved in cellular antioxidant and anti-inflammatory defense and mitochondrial protection. Lack of Fmr1 protein leads to an inhibitory effect on Nrf2 by E-cadherin. E-cadherin inhibits the relocation of Nrf2 to the nucleus and prevents Nrf2-dependent gene induction in the brain of *Fmr1* KO mice. *In vivo* treatment with NNZ-2566 exhibits a knockdown effect on E-cadherin normalizing the inducible activity of Nrf2.

Conclusions: NNZ-2566 reverses key molecular and cellular features and normalizes behavioral and anatomic aspects of the of the *fmr1* KO phenotype.

**147.002** A model for neural development and treatment of Rett syndrome using human induced pluripotent stem cells. C. Carromeu*, *University of California San Diego*

Background: The human brain is an intricate circuit of specialized neural cells. A disturbance in the homeostasis of this circuit can lead to various neuronal pathologies, including neurodevelopmental disorders. In such cases, the unavailability of affected human neurons for research has hampered the elucidation of disorder etiologies. Induced Pluripotent Stem Cells (iPSC) represent a rapidly evolving technology with great potential in areas ranging from basic research to drug discovery. When applied to neurodevelopmental disorders, the iPSC technology allows for the derivation of patient-specific neurons.

Objectives: Here, we use iPSCs to model Rett Syndrome (RTT) in vitro, a neurodevelopmental condition under the umbrella of the Autism Spectrum Disorders.

Methods: N/A

Results: The comparison of human RTT and non-affected neurons has generated insights into the

molecular and cellular mechanism of the disease, such as a deficit in synaptogenesis. Moreover, we used new techniques to measure neuronal network connectivity of iPSC-derived neurons in a dish. Our data display a network connectivity deficit and excitatory/inhibitory neurons imbalance in RTT neuronal cultures, compared to controls. Interestingly, most of these phenotypes can be rescued by the use of IGF-1, a molecule currently in clinical trial to RTT.

Conclusions: Our work with iPSC-derived cells suggests that therapeutic interventions using IGF-1 may be beneficial for RTT and possibly other neurodevelopmental disorders with similar phenotypes.

**147.003** Insulin-like growth factor-1 rescues synaptic and motor deficits in a mouse model of autism and developmental delay. J. D. Buxbaum*, *Icahn School of Medicine at Mount Sinai*

Background: Haploinsufficiency of SHANK3, due to either hemizygous gene deletion (termed 22q13 deletion syndrome or Phelan-McDermid syndrome) or to gene mutation, accounts for about 0.5% of the cases of autism spectrum disorder (ASD) and/or developmental delay, and there is evidence for a wider role for SHANK3 and glutamate signaling abnormalities in ASD and related conditions. Therapeutic approaches that reverse deficits in SHANK3-haploinsufficiency may therefore be broadly beneficial in ASD and in developmental delay.

Objectives: Investigate the effects of IGF1 on molecular, cellular, and behavioral abnormalities in mice haploinsufficient for Shank3.

Methods: Electrophysiology, molecular biology, biochemistry.

Results: We observed that daily intraperitoneal injections of human insulin-like growth factor 1 (IGF-1) over a 2-week period reversed deficits in hippocampal α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) signaling, long-term potentiation (LTP), and motor performance that we had previously reported in Shank3-deficient mice. Positive effects were observed with an IGF-1 peptide derivative as well.

Conclusions: We observed significant beneficial effects of IGF-1 in a mouse model of ASD and of developmental delay. Studies in mouse and human neuronal models of Rett syndrome also show benefits with IGF-1, raising the possibility that this compound may have benefits broadly in ASD and related conditions, even with differing molecular etiology. Given the extensive safety data for IGF-1 in children with short stature due to primary IGF-1 deficiency, IGF-1 is an attractive candidate for controlled clinical trials in SHANK3-deficiency and in ASD.

**147.004** IGF1 restore synaptic deficits in neurons from Phelan-McDermid syndrome patients. O. Shcheglovitov*[1], O. Shcheglovitova[1], M. Yazawa[1], T. Portmann[1], R. Shu[1], V. Sebastiano[1], A. Krawisz[1], W. Froehlich[1], J. A. Bernstein[2], J. F. Hallmayer[1] and R. Dolmetsch[3], (1)*Stanford University School of Medicine*, (2)*Stanford University*, (3)*Novartis Institutes for Biomedical Research*

Background: Phelan-McDermid Syndrome (PMDS) is a complex neurodevelopmental disorder characterized by global developmental delay, severely impaired speech, intellectual disability, and an increased risk of Autism Spectrum Disorders (ASDs). PMDS is caused by heterozygous deletions of chromosome 22q13.3. Among the genes in the deleted region is *SHANK3*, which encodes a protein in the postsynaptic density (PSD). Rare mutations in *SHANK3* have been associated with idiopathic ASDs, non-syndromic intellectual disability, and schizophrenia. Although *SHANK3* is considered to be the most likely candidate gene for the neurological abnormalities in PMDS patients, the cellular and molecular phenotypes associated with this syndrome in human neurons are unknown.

Objectives: To investigate cellular and molecular phenotypes associated with PMDS in human neurons.

Methods: We generated induced pluripotent stem cells (iPSCs) from individuals with PMDS and autism and used them to produce functional neurons. We then use elctrophysiology, biochemistry, and molecular biology to characterize the properties of iPSC-derived neurons.

Results: We show that PMDS neurons have reduced Shank3 expression and major defects in excitatory but not inhibitory synaptic transmission. Excitatory synaptic transmission in PMDS neurons can be corrected by restoring Shank3 expression or by treating neurons with insulin-like growth factor 1 (IGF1). IGF1 treatment promotes formation of excitatory

synapses that lack Shank3 but contain PSD95 and NMDA receptors with fast deactivation kinetics.

Conclusions: Our findings provide direct evidence for a disruption in the ratio of cellular excitation and inhibition in PMDS neurons, and point to a molecular pathway that can be recruited to restore it.

## 148 Genetics

*Organizer:* J. Veenstra-Vander Weele *Vanderbilt University*

**148.001** Convergence of Genes and Cellular Pathways Dysregulated in Autism Spectrum Disorder. D. Pinto*[1], C. Betancur[2], S. W. Scherer[3] and .. The Autism Genome Project Consortium[4], (1)*Icahn School of Medicine at Mount Sinai, 10029*, (2)*INSERM U952 - CNRS UMR 7224 - Universite Pierre et Marie Curie*, (3)*University of Toronto*, (4)*Autism Genome Project Consortium*

Background: Rare copy number variation (CNV) is an important source of risk for autism spectrum disorders (ASDs).

Objectives: This work represents the latest phase of the international Autism Genome Project Consortium's (AGP) effort to fully delineate the impact of CNV in ASD.

Methods: We assessed the impact of *de novo*and inherited rare CNV in a total of 2,446 ASD cases and their parents from the AGP along with 2,640 unrelated controls by applying a series of approaches to prioritize variants and key candidate ASD genes disrupted by CNVs, and to identify biological relationships and common pathways shared among those key genes. We have also integrated the latest exome sequencing data in downstream pathway studies.

Results: We confirmed an excess of genic deletions and duplications in cases over controls (1.41 fold, $p=1.0x10^{-5}$) and an increase of cases carrying exonic pathogenic CNV overlapping known dominant or X-linked ASD and intellectual disability loci (odds ratio=12.62, $p=2.7x10^{-15}$). Pathogenic CNVs, often showing variable expressivity, included rare *de novo* and inherited events at 36 loci, implicating novel ASD genes previously linked to other disorders (*CHD2*, *HDAC4* and *GDI1*), as well as novel genes such as *SETD5*, *MIR137* and *HDAC9*. Consistent with hypothesized gender-specific modulators, females with ASD were more likely to have highly-penetrant CNVs (p=0.017) and were also over-represented amongst cases with fragile X syndrome protein targets (p=0.02). Genes affected by *de novo* CNVs and/or loss-of-function single nucleotide variants converged on networks related to neuronal signalling/development, synapse function and chromatin regulation.

Conclusions: Collectively, these data inform clinical genetics interpretations, implicate specific neurobiological pathways and identify targets for therapeutic intervention.

**148.002** Epidemiology of Consanguineous Families in Autism. K. Schmitz-Abe*, M. Chahrour, T. W. Yu, C. A. Walsh and K. Markianos, *Boston Children's Hospital*

Background: Analyses of large autism datasets have provided statistical and functional evidence for the role of rare point mutations and transmitted and *de novo* copy number variants (CNVs), and offer crucial insights into the diverse genetic mechanisms that can lead to Autism Spectrum Disorders (ASDs).

Objectives: Ascertainment can point to differences in the underlying genetic mechanisms that lead to Autism. We subdivide families using two categories based on number of affected individuals and overall homozygosity. The two categories serve as a remarkably effective proxy for the underlying genetics. While the number of affected individuals, siblings as well as first-degree relatives, correlates strongly with severity of phenotype and M/F ratio, the level of homozygosity distinguishes between inherited and sporadic ASD.

Methods: We present homozygosity-CNV analysis for a cohort of 183 consanguineous families with one or more children affected with ASD 9 (HMCA). We follow up findings and draw comparisons with additional large ASD and control datasets: the Simons Simplex (SSC) and the Autism Genetic Resource Exchange (AGRE) collections (2,670 affected individuals; 9681 total individuals).

Results: We observe excess homozygosity among affected individuals relative to their unaffected siblings. The same trend is present in two additional, independent samples: the SSC and AGRE collections enriched respectively for sporadic and inherited causes of ASD. We apply a formal test based on family quartets to evaluate excess homozygosity showing the same results. A

plausible genetic mechanism driving excess homozygosity among affected individuals is the presence of homozygous copy number variation. We show for the first time conclusive evidence that double deletions contribute significantly to ASD.

Conclusions: Specifically, we find that *de novo* CNVs play a significant role in non-consanguineous families with a single affected child (p=0.04), but a lesser role in multiplex families, and they are no more common in ASD cases than controls in multiplex consanguineous families. In contrast, we present the strongest statistical evidence (p=0.013) to date that homozygous deletions, are a major contributor to ASD disease burden in consanguineous families, contributing to as much as 5-10% of cases. An additional line of evidence pointing to inherited factors for ASD in consanguineous families is the M/F ratio. All data sets show a progressively smaller M/F ratio with additional evidence of familiarity. The most dramatic change in the M/F ratio occurs for families with a single affected child. In this case requiring that any relative, including parents, present with any form of intellectual disability reduce the M/F ratio for consanguineous as well as non-consanguineous families. However the rate of change is very different. For consanguineous families M/F drops from 8 to 3 while for non-consanguineous families from 7 to 5. It is far more likely that close relatives, most frequently parents, cousins and uncles, share just a single allele rather than two causative alleles required for recessive inheritance. Thus the far smaller impact of additional familiarity requirements in consanguineous families underscores the importance of recessive inheritance in families with high-observed homozygosity.

**148.003** Exome Sequencing of Extended Families with Autism Reveals Genes Shared Across Neurodevelopmental and Neuropsychiatric Disorders.

H. N. Cukier*[1], N. D. Dueker[1], S. H. Slifer[2], P. L. Whitehead[2], E. Lalanne[1], N. Leyva[1], I. Konidari[2], R. C. Gentry[1], W. F. Hulme[2], D. Van Booven[2], V. Mayo[1], N. Hofmann[1], M. A. Schmidt[2], E. R. Martin[2], J. L. Haines[3], M. L. Cuccaro[2], J. R. Gilbert[2] and M. A. Pericak-Vance[2], (1)*University of Miami*, (2)*University of Miami Miller School of Medicine*, (3)*Case Western Reserve University*

Background: Autism spectrum disorders (ASDs) encompass a constellation of devastating neurodevelopmental conditions and studies to date demonstrate that the underlying etiology is extremely heterogeneous. With the advent of whole exome sequencing (WES), studies have been rapidly identifying genetic causes of many Mendelian disorders. Thus far, autism exome studies have primarily focused either on simplex families to discover *de novo*alterations or consanguineous families that carry recessive mutations.

Objectives: Our study performs exome sequencing in extended, multiplex families with affected cousin pairs to identify potential new ASD loci. We hypothesized that identical by descent (IBD) filtering in large, multiplex pedigrees would permit us to isolate genes contributing to ASD susceptibility. These extended families are likely to carry rare and partially penetrant alterations that are inherited to affected individuals from common ancestors.

Methods: We performed WES on at least two affected cousins across 40 multiplex ASD families to identify rare, segregating mutations that are incompletely penetrant. A total of 164 individuals were captured with the Agilent SureSelect Human All Exon kit, sequenced on the Illumina HiSeq 2000, and the resulting data processed and annotated with BWA, GATK, and SeattleSeq. Variants were filtered to those in IBD regions delineated by SNP genotyping data. Initial analyses focused on novel and rare (MAF < 0.05) variants predicted to be detrimental, either by altering amino acids or splicing patterns. Validation was performed by Sanger sequencing and genotyping on the Infinium HumanExome BeadChip.

Results: Following exome sequencing, each extended family had changes at approximately 90,000 locations. Variants were filtered to those in identity by descent (IBD) regions delineated by SNP genotyping data. Initial analyses focused on novel and rare (MAF < 0.05) variants predicted to be detrimental, either by altering amino acids or splicing patterns. In accordance with a dominant model of inheritance, exome sequencing identified 742 heterozygous changes and 3 potentially X-linked alterations; 502 variants were validated either by Sanger sequencing or genotyping on the Infinium HumanExome BeadChip. We identified numerous potentially damaging, ASD associated risk variants in genes previously unrelated to autism. A subset of these genes has been

implicated in other neurological disorders including depression (*SLIT3*), epilepsy (*CLCN2*), mental retardation (*AP4M1*, *CEP290*), schizophrenia (*WDR60*), and Tourette syndrome (*OFCC1*). This reinforces the theory that there are shared genetic components across distinct neurological disorders. We also found additional alterations in previously reported autism candidate genes (*NRXN2, PRICKLE1,* and *SYN1*) including three genes with alterations in multiple families (*CSMD1*, *FAT1*, and *STXBP5*), thereby expanding the evidence that these genes are involved in autism etiology. Compiling a list of ASD candidate genes from the literature, we determined that variants occurred in ASD candidate genes 1.65 times more frequently than in random genes captured by exome sequencing ($p=8.55x10^{-5}$).

Conclusions: By studying these unique pedigrees, we have identified novel DNA variations related to ASDs, demonstrated that exome sequencing in extended families is a powerful tool for ASD candidate gene discovery, and provided further evidence of an underlying genetic component to a wide range of neurodevelopmental and neuropsychiatric diseases.

**148.004** Fragile X, Intermediate, and Premutation Alleles in the Autism Genetic Resource Exchange (AGRE). W. T. Brown*[1], A. Glicksman[2], X. H. Ding[1], N. Ersalesi[2], C. Dobkin[2] and S. Nolin[1], (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*New York State Institute for Basic Research in Developmental DIsabilities*

Background: AGRE is an autism family registry and resource that includes primarily multiplex families, having two or more children affected by autism spectrum disorders. Family pedigree, phenotypic and genotypic data are available online, and genetic material is available. The families were recruited by ads and contact with local support groups by Cure Autism Now and Autism Speaks. They represent a relatively unbiased sample.

Objectives: To determine the incidence of Fragile X Full, Intermediate, and Premutations in the cohort.

Methods: We screened the FMR1 locus in one proband from each of 1795 families.

Results: We found 8 families that had the fragile X mutation present. 35% of the first 480 families were noted to have had some genetic testing prior to entering the registry. Among these, 6 were found among the first set of 480 families. The prevalence of fragile X among the ~312 AGRE families that had had no prior genetic screening was ~ 1.9%. An estimate of the IQ score of the autistic subjects was 80±35 with range 34-144, based on Raven and Stanford-Binet testing. Thus, the AGRE sample is likely to have a higher IQ distribution than typical for fragile X subjects (mean ~40±25). Previous prevalence studies of fragile X in autistic samples range from 0 to 16%; with a mean of ~4%; (Feinstein 98). Our 1.9% is similar to a report of 1.6% among 123 unrelated autistic individuals (Bailey 93), but lower than the 13% we found on an earlier multicenter study of 183 individuals (Brown 86).

**We tested to see if there is an association of autism and permutations or intermediate alleles.** Among the 1535 male probands tested, there were 2 with premutation (59 & 64 CGGs) and 12 with intermediate (45-54 CGGs) alleles (46, 47, 47, 47, 48, 48, 48, 49, 50, 50, 51, 54) for an intermediate prevalence of 0.76%. Among the 211 female probands tested there were 2 with premutations (55, 59) and 7 with intermediate alleles (45, 46, 48, 50, 52, 53, 54). Since females have two alleles, dividing by 2 gives an intermediate allele prevalence of 1.7% in female alleles or an overall intermediate allele prevalence of 0.86%. Our published control value for 2500 X chromosomes was 1.7% (Brown 96), and our more recent control value based on carrier screening of 9064 X chromosomes was 1.15%.

Conclusions: A growing awareness of fragile X syndrome has decreased the probability of fragile X in these multiplex autism families due to screening and exclusion from AGRE. The observed frequency of 1.9% in the first 480 families was lower than the expected 4%, perhaps due to higher IQs in AGRE subjects than is typical for fragile X. This finding confirms an association of fragile X and autism.

There was no excess of intermediate or premutation alleles among the AGRE registry autistic probands. **This finding suggests autism is NOT associated with intermediate (45-54) or premutation (55-200) alleles**.

**148.005** Genotype Phenotype Correlation in Patients with Synaptic Genes Mutations. F. Bonnet-Brilhault*[1], M. Gomot[2], R.

Blanc[3], C. Destrieux[4], S. Bazaud[4], C. Andres[4], S. Alirol[4], A. Toutain[4], M. Raynaud[4] and F. Laumonnier[1], (1)*UMR 930 Inserm-Universite Francois Rabelais Tours*, (2)*INSERM U930*, (3)*INSERM U 930*, (4)*INSERM*

Background: The phenotypical heterogeneity is observed in ASD even in patients carrying gene mutations in the same gene. In 2004 and 2009 we reported two ASD cases, one familial and one sporadic, carrying a deleterious different mutation in the NLGN4X gene (Laumonnier et al, 2004; Daoud et al, 2009).

Objectives: To evidence genotype phenotype correlation in patients carrying NLGN4X gene mutations.

Methods: We performed the whole exome sequencing (WES) of these 2 individuals with ASD and 1 uncle. Phenotypic characterization of patients and relatives included behavioural, cognitive, electrophysiological and MRI evaluations.

Results: We discovered a second truncating mutation affecting either (i) the *GLRB* gene encoding a postsynaptic receptor interacting with *NLGN4X* in the family described in Laumonnier *et al (2004)*, (ii) or the *MLL3* gene, previously involved in ASD/ID, for the sporadic case (Daoud et al, 2009). The combination of the *NLGN4X* mutation and the second truncated gene was specific to patients with ASD and was absent in controls as well as relatives with ID only . Complete phenotypic evaluation of the pedigrees has evidenced within these two ASD cases common autistic behavioural features and neurophysiological pattern (*ie* abnormal Mismatch Negativity on auditory ERP) but different developmental trajectories and cognitive profiles. Furthermore the ASD case within the multiplex family had a different cognitive profile from members carrying the *NLGN4X* mutation only.

Conclusions: These results illustrate, to our knowledge, for the first time that the phenotypic variability present in ASD multiplex families or in different families that include patients having a similar deleterious mutation in a candidate gene (such as *NLGN4X*), is caused by the combinatory effect of at least a second mutation in another gene.

**148.006** Integrated Analyses of Genome Wide Association and Targeted Sequencing Data Identify Loss of Function and Noncoding Regulatory Rare Variants Contributing to Autism Spectrum Disorder.

A. J. Griswold*[1], N. D. Dueker[1], D. Van Booven[1], J. A. Rantus[2], J. Jaworski[1], S. H. Slifer[1], M. A. Schmidt[1], W. F. Hulme[1], I. Konidari[1], P. L. Whitehead[1], S. M. Williams[3], R. Menon[4], M. L. Cuccaro[1], E. R. Martin[1], J. L. Haines[5], J. R. Gilbert[1], J. P. Hussman[6] and M. A. Pericak-Vance[1], (1)*University of Miami Miller School of Medicine*, (2)*University of Miami*, (3)*Vanderbilt University*, (4)*Emory University*, (5)*Case Western Reserve University*, (6)*Hussman Foundation*

**Background:** Genome-wide association studies (GWAS) and exome sequencing have found no single common or rare factor accounting for the genetic risk for autism spectrum disorders (ASD). This leads to the hypothesis that genetic variants in hundreds of genes and nongenic loci contribute to ASD. Identification of such rare risk variants by sequencing large cohorts for rare or low frequency variants with potential functional significance to ASD is essential.

**Objectives:** To identify rare coding and noncoding ASD risk variants integrating GWAS association with custom targeted massively parallel sequencing of candidate regions.

**Methods:** Candidate regions were chosen from GWAS Noise Reduction analyses of two autism datasets (Hussman et. al., 2011). We sequenced 17Mb on the Illumina HiSeq2000 utilizing a custom Agilent SureSelect probe-set targeting exons, UTRs, conserved intronic areas, and regulatory regions of 681 GWAS-NR associated genes and conserved regions in 694 associated intergenic loci. Our cohort consisted of 2,112 ASD cases and 834 controls of white ethnicity determined by Eigenstrat. Bioinformatic processing included alignment with bwa, genotype calling with the GATK Universal Genotype Caller, and annotation of coding variants with SeattleSeq137, PolyPhen2, and SIFT and noncoding variants with ENCODE, VISTA, and GENCODE databases. We first identified rare (MAF≤0.01) loss-of-function (LOF) alterations (stop gains-losses, splice changes, and frameshifts) or genes with multiple damaging variants in the same individual, and noncoding variants predicted likely to affect binding by RegulomeDB. For LOF variants in ASD candidate genes, we determined inheritance status of the variant by Sanger sequencing. We used the Sequence Kernel Association Test (SKAT) for gene and noncoding element based association testing between sets of rare variants and ASD.

**Results:** We identified 547,716 single nucleotide variants (SNVs) and 94,326 indels, including 29,734 coding variations and 2,653 rare LOF alterations. No overall difference existed between cases and controls in the number of variations or multiple hit genes, but there was significant enrichment in cases when restricting to LOF variants in ASD candidate genes (p=0.003). Among these was a confirmed *de novo* premature stop in the candidate gene *RBFOX1.* RegulomeDB predicted 55 case unique noncoding variants to affect transcription factor binding motifs. Two were in the same glutamate receptor gene, *GRIK4*, altering SP1 and CTCF sites. Association testing identified only nominally significant associations with rare exonic variants ASD in 30 genes including the transcription factors *ZNF24* (p=0.00192) and ZNF519 (p= 0.00465) and nominal significance with rare SNVs in enhancer hs658 (p=0.07) that drives expression in the midbrain of mouse embryos. Further analyses of subsets of variations are ongoing.

**Conclusions:** The identification of an enrichment of LOF variants in ASD candidate genes corroborate literature from other ASD datasets and identification of a *de novo* LOF in *RBFOX1* further establishes its importance as an ASD gene. As the first large scale study of noncoding variation in ASD, this investigation adds noncoding variants to the compendium of ASD risk loci and implicate potential novel biological mechanisms contributing to ASD etiology. Overall, this study highlights integration of association and sequencing data to find rare ASD risk alleles.

**148.007** Leveraging Hyperserotonemia and Whole Exome Sequencing in Autism Spectrum Disorder Families to Tackle Genetic Heterogeneity. J. S. Sutcliffe*[1], N. G. Campbell[1], E. L. Crawford[1], V. Trubetskoy[2], A. Rodriguez[2], R. Madduri[2], B. Li[1], L. K. Davis[2], N. J. Cox[2] and E. H. Cook[3], (1)*Vanderbilt University*, (2)*University of Chicago*, (3)*University of Illinois at Chicago*

Background: Autism spectrum disorder (ASD) is characterized by a complex and extremely heterogeneous genetic etiology. Numerous lines of investigation implicate serotonergic dysfunction in ASD. Examples include hyperserotonemia, or significantly elevated levels of platelet serotonin (5-HT) in ~35% of cases, and (2) efficacy of selective serotonin reuptake inhibitors in ameliorating anxiety and irritability related to insistence on sameness (IS) and other rigid-compulsive behaviors (RCBs). Notably, platelet serotonin is itself highly heritable, and correlation of hyperserotonemia with OCD in first-degree relatives has been documented. Common variants individually show small effects on risk, yet in aggregate, common genetic variation contributes significantly to heritability. Both CNV and whole exome sequencing (WES) point to de novo and inherited rare variants (RVs) as a major class of autism risk.

Objectives: We hypothesized that examination of WES data in autism families identified as having hyperserotonemic probands will reduce genetic heterogeneity and offer insight into ASD risk, specifically relevant to serotonergic dysfunction.

Methods: To tease out genetic factors related to RCBs and also hyperserotonemia as a heritable biomarker in ASD, we conducted WES of families selected on the basis of these traits. While most families were parent-child trios, one was a large 4-generation, multiplex family with several affected members across generations. In addition to filtering WES data for de novo mutations (DNMs), partially reported in Neale et al 2012, we also filtered phased family exome data to identify autosomal or X-linked genes harboring inherited compound heterozygous (CH; '2-hit'), or X-lined hemizygous (in males) 'functional' variants (missense, nonsense, consensus splice site and read-through). A gene-collapsing transmission disequilibrium test (cTDT) was employed to explore potential over-transmission of RVs in conjunction with a Consensus Genotyper for Exome Sequence (CGES) to improve call accuracy and reduce the artifactural bias towards an excess of observed non-transmissions. Finally, various algorithms and multiple databases were used to explore gene/protein network enrichment.

Results: Numerous loci were identified to harbor 'functional' CH genotypes and DNMs. Various analyses indicated an enrichment of genes so identified in pathways related to cell adhesion, extracellular matrix proteins and genes previously implicated in ASD, intellectual disability or other neurological phenotypes. Analysis of the multiplex family revealed twelve functional variants shared across all affected members and obligate ('unaffected') carriers. As expected, there is a bias towards larger genes harboring such variants, but pathway enrichment nevertheless suggested

biological relevance. TDT analysis initially showed an expected over-representation of genes harboring non-transmitted functional variants, reflecting false negative calls in probands or false positive calls in parents. The application of multiple genotype calling algorithms in the cloud-based CGES dramatically improves genotype call metrics and reduces bias towards overall under-transmission. We are working across the board to integrate functional rare variants and CNVs in all families.

Conclusions: We have used a hyperserotonemic and RCB-selected subset of ASD to identify potential risk factors in ASD and have found numerous genes harboring 'functional' de novo mutations, inherited two-hit, compound heterozygous variants and CNVs that provide clues into specific gene sets and functional pathways of relevance.

**148.008** Phenotypic Profile of Children with ASD with Gene Disruptions in the Beta-Catenin Pathway. R. K. Earl*[1], J. E. Elgin[2], T. Ward[2], A. Stevens[1], J. Gerdts[1] and R. Bernier[1], (1)*University of Washington*, (2)*University of Washington Autism Center*

Background: Autism spectrum disorder (ASD) is a genotypically and phenotypically complex disorder. Gene disruptions within the beta-catenin pathway have been associated with ASD (O'Roak et al, 2012). Beta-catenin plays a critical biological role in cell growth and differentiation, and is believed to be involved in synaptic formation as well as memory and learning processes (Maguschak & Ressler, 2012). Understanding the phenotypic profile that accompanies genetic mutations in this specific pathway can help to tease apart potential ASD subtypes that arise from different genetic disruptions.

Objectives: To explore the cognitive and behavioral phenotype as well as gender distribution of individuals with ASD who have a gene disruption in the beta-catenin pathway compared to affected individuals without this pathway mutation.

Methods: Participants were 2557 children meeting strict criteria for ASD. 94 children (29 female) with disruptive mutations falling in a protein network within the beta-catenin pathway were compared to 2151 children (312 female) without gene disrupting mutations in this network. Groups were compared on nonverbal (NVIQ) and verbal IQ (VIQ), as well as parent-reported and clinician-observed measures of social impairment and repetitive behaviors as a function of gender.

Results: Groups differed in gender rate, with a higher rate of females in the beta-catenin pathway group than the non-pathway group ($c^2(1, N=2557) = 25.9$, $p<.001$). Children in the pathway group had lower nonverbal and verbal IQ scores relative to the non-pathway group (NVIQ: $F(1,2552) = 21.7$, $p<.001$, $\eta^2=.008$; VIQ: $F(1,2552) = 6.56$, $p=.010$, $\eta^2=.003$). There was an interaction between pathway status and gender, indicating a trend toward increased social impairment in males in the pathway group and no differences in females across groups ($F(1,2421)=4.19$, $p=.041$, $\eta^2=.002$).

Conclusions: Higher rates of females in the beta-catenin pathway group replicate previous findings of higher incidence of genetic mutations and copy number variations in females with ASD (Marshall et al, 2008). The phenotype of children with beta-catenin pathway disruption is characterized by significantly greater cognitive impairment and increased social impairment in males, echoing beta-catenin's role in memory, learning, and socioaffective processes. Phenotypic subtyping such as this is a promising way to illuminate genotypic variations amongst individuals with ASD.

**148.009** Paternal Age-Related Changes in DNA Methylation from an Autism-Enriched Cohort. J. I. Feinberg*[1], K. M. Bakulski[2], R. Tryggvadottir[1], S. C. Brown[2], A. E. Jaffe[3], L. R. Goldman[4], L. A. Croen[5], I. Hertz-Picciotto[6], C. J. Newschaffer[7], M. D. Fallin[2] and A. P. Feinberg[1], (1)*Johns Hopkins University*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Lieber Institute for Brain Development*, (4)*George Washington University School of Public Health and Health Services*, (5)*Kaiser Permanente Northern California*, (6)*UC Davis MIND Institute*, (7)*Drexel University School of Public Health*

**Background**: Age-related epigenetic changes have been proposed to contribute to common human disease. Autism has been suspected to be associated with increased paternal age but the exact biological mechanisms are yet unknown.

**Objectives**: We examined the hypothesis that DNA methylation (DNAm) in semen-derived DNA samples might show age-specific alterations in the

paternal genome with the intention that these might contribute to autism risk in offspring.

**Methods**: We performed comprehensive genome-wide DNAm analyses on DNA derived from semen samples contributed by fathers enrolled in the Early Autism Risk Longitudinal Investigation (EARLI) cohort. We analyzed methylation data from 50 samples run on the CHARM 3.0 array, which measures DNAm at over 7 million CpG sites, in addition to data from 42 samples run on the Illumina Infinium 450k platform (~480,000 CpG sites). A total of 32 samples were analyzed on both platforms. Next, we used a well-tested statistical algorithm to identify regions in the genome with age-dependent changes in DNAm.

**Results**: We identified differentially methylated regions (DMRs) of the paternal genome with significant age-dependent changes. Intriguingly, many of these regions contained genes enriched for neurodevelopmental pathways.

**Conclusions**: This is the first evidence for an age-related change in DNAm in semen, which may be a plausible potential mechanism for the paternal age association with ASDs. While autism outcomes in the offspring of this cohort will not be available for several years, the EARLI cohort provided a unique biological resource of fathers of high-risk siblings, and such ASD-related analyses from these age-associated epigenetic findings are planned.

## 149 Towards an Integrated Neurocognitive Account of Local Versus Global Visual Processing in Autism Spectrum Disorders

*Discussant:* D. R. Simmons *University of Glasgow*

*Organizer:* B. Boets *KU Leuven*

Atypical visual processing in autism spectrum disorders (ASD), such as superior processing of local details or substandard processing of global structures, has been investigated repeatedly, but research findings vary widely and are often contradictory. Here, we present a collection of behavioural and neuroimaging studies that investigate various levels of visual processing in individuals with ASD and well-matched typically developing (TD) controls. In particular, we aim to get a better understanding of the interrelation between local versus global visual processing, either by applying paradigms that try to disentangle the relative contribution of both types of processing or by applying paradigms that investigate the interplay between bottom-up and top-down processing. Findings generally indicate subtle group differences between individuals with ASD and TD individuals, which strongly depend on task-demands and stimulus characteristics. In line with the literature, this series of studies reveals a mixed pattern of results, ranging from evidence for a more locally oriented processing style and impaired global processing, towards intact and even enhanced global integration capacities in ASD. It is concluded that atypical visual processing cannot currently provide us with a reliable endophenotype for ASD.

**149.001** Evidence of global weakness in autism spectrum disorder. R. D. Booth* and F. Happe, *King's College London*

**Background**: In Frith's original description of weak central coherence, the assets and deficits seen in autism were thought to stem from a single cognitive characteristic. This implied that reduced global integration of information results in enhanced local processing. More recent accounts of this theory emphasize the role of superior local perception with independent, and possibly intact, global integration skills. However it is questionable whether the measurement of local and global processing is indeed independent, with most paradigms used to test weak coherence often placing local and global processing in direct trade-off. Typically it is not possible to determine whether patterns of performance in autism are a consequence of reduced global processing, increased local processing, or both.

**Objectives**: We aimed to design measures that tap global integration unconfounded with local processing bias.

**Methods**: Two novel measures of visual integration were designed: (1) a modified Fragmented Picture-Completion task which required participants to identify a picture from fragments and (2) an (Im)possible Figures task which required participants to judge whether three-dimensional figures could be geometrically possible. Performance on both measures were compared between 30 males with ASD and 30 controls, matched in age and IQ, as well as within a large typically developing population (N = 201).

**Results**: Poor integrative processing was found in the ASD group compared to 30 controls: participants with ASD required more completed fragments in order to identify an image and had lower sensitivity to impossibility. A relationship between sensitivity in discriminating possible and impossible figures and the incremental amount of

information required to detect fragmented pictures was found in the typically developing sample (N = 201, r = -.20 to -.30 which held after controlling for IQ and age). However no such relationship was found in the ASD and matched control groups.

**Conclusions**: Evidence of reduced global processing was found in individuals with ASD compared to matched controls, suggesting Frith's original notion of weak coherence as both reduced global integration and increased local perception is worth revisiting. However the role of perceptual integration versus cognitive flexibility for the theory of weak coherence also requires some consideration.

**149.002** Atypical visual processing as an endophenotype of autism spectrum disorders?. L. Van Eylen*, B. Boets, J. Steyaert, J. Wagemans and I. Noens, *KU Leuven*

**Background:** Autism spectrum disorders (ASD) are highly heritable, but insight into the underlying etiology is still limited, mainly due to considerable heterogeneity within ASD. This large heterogeneity stimulates the search for more 'genetically informative phenotypes' or 'endophenotypes' that allow us to delineate more homogeneous subgroups. Endophenotypes are phenotypes that are more proximal to the biological etiology of a clinical disorder than its signs and symptoms, and are influenced by one or more of the same genes that confer susceptibility to the condition. Accordingly, it is postulated that a good ASD endophenotype should co-occur with ASD and should be expressed at a higher rate in unaffected first-degree relatives of ASD probands than in the general population. Atypical visual processing has been suggested as a potential endophenotype for ASD. Enhanced local processing and reduced global processing abilities have been reported in ASD, as well as a more locally oriented processing style.

**Objectives:** The aim of this study is to assess which visual processing measures provide good endophenotype candidates for ASD.

**Methods:** In line with Booth (2006) four tasks were administered, targeting local versus global processing abilities at different levels (low- to mid-level versus higher-level visual tasks) and measuring processing style: a visual search task (local processing/low to mid-level), a coherent motion task (global processing/low to mid-level), a fragmented object outlines task (global processing/higher level) and the Rey-Osterrieth Complex Figure (processing style). Two reaction time tasks were also included to control for differences in motor speed. All tasks were administered from 315 individuals (IQ>70), covering five groups: children with ASD (n = 62), their first-degree relatives (unaffected siblings (n = 38) and parents (n = 91)), typically developing (TD) children (n = 63) and TD adults (n = 61). The age range in children and adults was 8-18 and 30-60 years, respectively.

**Results:** Analyses comparing children with ASD and TD children (matched for age, IQ and gender) showed a more locally oriented processing style and increased motion coherence thresholds in children with ASD. There were no significant group differences in visual search or motor speed. On the fragmented object outlines task, only subtle group differences were found, suggesting that participants with ASD needed slightly more information to correctly identify object contours. First-degree relatives of ASD probands did not perform differently from matched TD individuals.

**Conclusions:** Individuals with ASD showed a more locally oriented processing style, but no superior local processing ability, nor a general global processing deficit. Reduced global processing was only found on the coherent motion task, and only subtle differences were found on the fragmented object outlines task. Recent studies suggest that deficits on the coherent motion task may be due to a reduced ability to segregate signal from noise rather than reduced global integration. These findings, combined with the absence of group differences between ASD relatives and TD individuals indicate that visual processing abilities and visual processing style do not offer good endophenotypes for ASD.

**149.003** Local and global contributions to direction integration performance in children with autism spectrum disorder. C. Manning*[1], S. Dakin[2], M. Tibber[2], T. Charman[3] and E. Pellicano[4], (1)*Institute of Education*, (2)*University College London*, (3)*King's College London*, (4)*Centre for Research in Autism & Education, Institute of Education*

**Background:** Difficulties in global motion processing have often been reported in autism spectrum disorder (ASD), and have been interpreted as reduced integration of local motion signals in individuals with ASD. However, these findings have been almost exclusively based on

the motion coherence paradigm, which is not a pure measure of integration (Dakin & Frith, 2005). Indeed, elevated motion coherence thresholds could also arise from imprecision in estimating the direction of individual elements, as predicted by accounts of increased neural noise in ASD (Simmons et al., 2009). The equivalent noise paradigm (e.g., Dakin, Mareschal & Bex, 2005) allows the relative contributions of local and global processes to be separated, by providing independent estimates of local noise (i.e., imprecision in estimating the direction of individual elements) and global pooling (i.e., efficiency in averaging across local estimates).

**Objectives:** We sought to investigate whether elevated motion coherence thresholds in children with ASD can be attributed to atypical levels of local noise and/or atypical global pooling.

**Methods:** We presented an equivalent noise direction discrimination task and a motion coherence task in slow (1.5 deg/sec) and fast (6 deg/sec) speed conditions to children with ASD aged 6 to 13 years (n=23) and age- and ability-matched typically developing children (n=23). In both tasks, stimuli were unlimited lifetime random dot patterns presented for 400ms. In the equivalent noise task, two external noise conditions were interleaved. In the 'no noise' condition, the standard deviation of dot directions was 0 degrees, and the threshold was taken as the finest direction discrimination possible. In the 'high noise' condition, the mean dot direction was fixed at 45 degrees, and the maximum amount of tolerable noise was assessed. The thresholds from these two conditions were used to fit an equivalent noise function and estimates of local noise and global pooling were obtained. In the motion coherence task, a proportion of dots moved coherently leftwards or rightwards, and participants were asked to indicate the direction of coherent motion.

**Results:** Children with ASD had comparable motion coherence thresholds to typically developing children. Additionally, children with ASD had similar levels of local noise as typically developing children. Unexpectedly, however, children with ASD were able to globally average over *more* estimates than their typically developing peers.

**Conclusions:** Three important implications emerge from our results. First, our findings challenge the common assumption that children with ASD have difficulties with global motion integration and instead suggest that children with ASD integrate *more* efficiently than typically developing children. Second, our results suggest that previously reported difficulties in motion coherence tasks may be due to difficulties segregating signal from noise in individuals with ASD rather than reduced global integration. The fact that we did not find elevated motion coherence thresholds in the current study suggests that such difficulties may be dependent on specific task and stimulus parameters. Third, our results challenge accounts of increased neural noise in ASD, as children with ASD had similar estimates of local noise and tolerated more external noise compared to typically developing children.

**149.004** Components of visual perceptual organisation in ASD: An overview of behavioural and fMRI evidence using Gabor patterns. K. Evers*, R. Van der Hallen, B. Boets, B. Haesen, L. Van Eylen, J. Steyaert, I. Noens and J. Wagemans, *KU Leuven*

**Background:** An atypical perceptual style, with a more locally oriented default processing level and an attenuated bias for global processing, is often described in ASD. Although extensive research has been conducted to pinpoint the specific differences with typical development, the literature is highly mixed and therefore difficult to integrate into clear-cut findings. Several stimulus- and task-related aspects appear to contribute to this diversity in research findings.

**Objectives:** We performed a series of studies to evaluate the impact of stimulus- and task-related characteristics on visual perceptual organisation in individuals with ASD and typically developing controls. In particular, Study 1 and 2 investigated the influence of task instruction on perceptual organisation, Study 3 investigated the interplay between different processes involved in object identification, and Study 4 investigated the neural underpinnings of perceptual organisation in terms of texture segmentation and contour integration. All studies have in common that they used the same type of stimuli.

**Methods:** Three behavioural studies and one functional magnetic resonance imaging (fMRI) study were carried out. Participants were children

and adolescents with ASD and well-matched typically developing controls. All four studies used stimuli composed of Gabor patches, which are highly controllable elements inspired by the tuning properties of visual neurons. In Study 1 and 2 we investigated the influence of (explicit versus implicit) task instruction on perceptual organisation of meaningless stimuli. In Study 3 we used dynamic Gabor patterns that gradually evolved from random towards organised to investigate contour- and texture-based object identification. In Study 4, dynamically evolving Gabor patterns were used to investigate the neural mechanisms behind texture segmentation and contour integration of nonexistent and everyday objects using fMRI.

**Results:** The behavioural studies demonstrated the presence of certain task- and stimulus-specific effects in both participant groups (e.g., a beneficial effect of symmetry upon bottom-up perceptual grouping). Differences between participant groups were subtle and depended on task demands and stimulus characteristics. Whereas individuals with ASD performed similarly to controls in a simple object detection task (Study 4), they performed more poorly in object identification, especially when more complex objects were presented (Study 3) or when implicit task instructions were given (Study 1). The fMRI findings revealed that more structured Gabor patterns systematically activated hierarchically higher areas along the ventral visual stream. However, the pattern of brain activity was similar for both groups.

**Conclusions:** No overall problems in visual processing were found in ASD. Instead, we tapped into some subtle aspects of the (a)typical visual processing style of individuals with ASD and showed the differential effect of task demands and stimulus characteristics on perceptual organisation. This set of paradigms where participants are required to make sense of changing visual input with variable levels of noise and structure, suggests that the peculiarities in ASD are situated in the interplay between bottom-up and top-down processes. Thus far, the brain imaging data did not provide evidence for atypical neural processing in ASD, but the subtraction-based analyses will be complemented with structural and functional connectivity analyses, evaluating the efficiency of communication between brain regions.

## 150 Early Atypical Growth Patterns in ASD: Evidence from Behavioral, Neuroimaging, and Neurobiological Studies

*Discussant:* E. DiCicco-Bloom *Robert Wood Johnson Medical School*

*Organizer:* K. Chawarska *Yale University School of Medicine*

Brain over-growth in infancy is one of the best-replicated imaging findings in ASD. Considering the high correlation between HC and total brain volume, particularly in infancy, atypical HC trajectory may also provide a proxy for abnormal brain development during infancy. Even though early brain growth and, more generally, early somatic overgrowth is well-recognized in ASD, the underlying biological mechanisms and relationships to the etiology of ASD remain poorly understood. The proposed symposium will address a number of key questions regarding early overgrowth in ASD, including its prevalence and effects of gender on growth patterns, evidence from neuroimaging studies of infant siblings of children with ASD, animal models of autism risk factors, as well as studies modeling neuronal growth using induced pluripotent stem cells.

**150.001** Early Head and Body Overgrowth in Boys and Girls with ASD: Prevalence Rate and Clinical Outcomes. D. J. Campbell*[1], J. Chang[2] and K. Chawarska[1], (1) *Yale University School of Medicine*, (2) *Yale University*

Background:

Brain enlargement in infancy, recently reported to occur in association with an generalized overgrowth in physical stature, is one of the best-replicated biological findings in ASD. It is not clear whether generalized overgrowth is also present in girls, what its prevalence is, and whether it is associated with clinical outcomes in childhood.

Objectives:

To examine: somatic growth in boys and girls with ASD compared to a community sample of typically developing (TD) children; prevalence of generalized overgrowthin ASD and TD infants; and predictive association between generalized overgrowth and clinical phenotype at 4 years.

Methods:

Head circumference (HC) as an indirect measure of brain size in infancy, height, and weight measurements were collected retrospectively from 200 children (161M/39F) with ASD and 147

typically-developing (TD) controls (98M/49F) between birth and 24 months of age. Growth curves for each measure were modeled using splines. The three measures were combined using principal components analysis to obtain a generalized overgrowth component (PC1). Prevalence rates of macrocephaly were estimated by the proportion of children with HC scores 2 SD above/below the TD mean; macrosomy rates were estimated similarly using PC1 scores. Extreme generalized and HC growth rates were estimated by the proportion exceeding 2 SD above the mean in change between birth and 24 months in TD group. Social, developmental, and adaptive functioning was measured at 2 and 4 years.

Results:

Generalized overgrowth was more pronounced in boys than in girls with ASD. Extreme overgrowth from birth to 2 years was present in 16% of the ASD toddlers as compared to 3.4% in TD controls ($p$<.001); at 2 years. Corresponding estimates were similar when only HC growth was considered: extreme HC overgrowth was noted in 15.0% of toddlers with ASD but only 3.4% of TD controls ($p$ < .001). At 24 month 6.5% of toddlers with ASD had macrocephaly compared with 4.1% of TD controls (p= .47). Within ASD group, larger body size at birth predicted lower verbal ($p$=.01), nonverbal ($p$=.005), and adaptive communication ($p$=.02) skills and higher autism severity ($p$=.02) at 4 years. Accelerated somatic postnatal growth contributed to poorer verbal ($p$=.005), nonverbal ($p$=.01), adaptive communication ($p$=.007), and repetitive behavior ($p$=.002) scores at 4 years after controlling for body size at birth.

Conclusions:

Co-occurrence of accelerated skeletal and HC growth in ASD suggests a common mechanism, potentially constraining the search for underlying biological factors. Girls are less likely to exhibit overgrowth than boys, though factors related to such dimorphism remain unknown. Although early growth abnormalities in ASD are less common than previously thought, their presence is predictive of clinical outcome at 4 years. Future studies will elucidate pre- and postnatal factors affecting growth in ASD and determine whether the generalized overgrowth endophenotype plays a role in etiology of the disorder and reveals novel treatment targets.

**150.002** Longitudinal Head Circumference and Accelerated Brain Growth in Infants at Risk for Autism. H. C. Hazlett*[1], H. Gu[2], M. A. Styner[1], J. Piven[1] and .. The IBIS Network[3], (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina*, (3)*Autism Center of Excellence*

Background: There has been a range of findings on head circumference in populations with autism spectrum disorders (ASD). Independent studies have identified increased head circumference, no difference in head circumference, and even smaller head circumference in ASD samples. Difficulties in understanding the discrepancy of these results come from the heterogeneity of samples (e.g., severely impaired vs. higher functioning), the nature of the comparison group (e.g., normative data vs. local controls), and the paucity of true longitudinal studies.

Objectives: To characterize head circumference trajectories from 6 to 24 months in a large longitudinal sample of infant siblings at high familial risk for ASD.

Methods: Head circumference data was obtained from The Infant Brain Imaging Study (IBIS). The IBIS Network is an NIH-funded Autism Center of Excellence following a cohort of high risk (HR) and low risk infants from 6 months of age. Participants received developmental and behavioral assessments and MRI scans at 6, 12, and 24 months. Classification for ASD occurred at the 24 month visit, using DSM-IV and ADOS diagnostic criteria to determine which HR infants met criteria for ASD. Low risk infants were negative for ASD and had no first degree relatives with an ASD. Three groups were examined for our analyses: 36 HR-ASD, 150 HR-non ASD, and 87 low risk infants. Automated measures of head circumference were obtained directly from the MRI scans. Data were analyzed using longitudinal random coefficient growth curve models controlling for sex, length, and cognitive developmental level (from the Mullen).

Results: We observed a trend for group differences in the trajectory of head circumference from 6 to 24 months, although this was only marginally significant ($p$ = .05). Cross-sectional comparisons found that the HR-ASD group had significantly increased head circumference at 24 months ($p$=.04), but did not look different from

the other two groups at 6 or 12 months. However, brain overgrowth was evident in this group, with the HR-ASD group showing a significantly accelerated rate of growth (e.g., intracranial volume, $p$ = .02).

Conclusions: Increased brain volume and head circumference was present by 24 months in HR-ASD infants, but not at 6 or 12 months of age, suggesting an underlying postnatal mechanism involving brain overgrowth. These findings indicate that in a high risk population, increased head circumference may not be observed before age 2, but that accelerated rates of brain volume growth can be detected in infants later identified with ASD. Interestingly, these trajectories appear to be aligned with the emergence of clinical symptoms. Since head circumference is only a proxy for brain volume, neuroimaging studies focused on understanding the underlying neurobiology of autism may provide the best information about possible mechanisms of early brain overgrowth.

**150.003** Genome and Transcriptome Analyses of Induced Pluripotent Stem Cells in ASD. F. Vaccarino*, J. Mariani and G. Coppola, *Yale University School of Medicine*

Background: Increased brain size and larger head circumference (macrocephaly) characterizes as many as 20% of children with autism spectrum disorders and confers poorer outcome.

Objectives: To understand the neurobiology of ASD, we derived induced pluripotent stem cells (iPSCs) from 5 children with ASD and macrocephaly and their unaffected family members.

Methods: IPSCs are pluripotent cells that can be differentiated into any other cell of the body, including neurons. Because iPSCs and their progeny maintain the genetic characteristics of the individual of origin, these cells represent a promising model for diagnostics, drug discovery, therapeutics and personalized medicine.

Results: Our dataset currently comprises 45 iPSC lines obtained from 15 individuals in 5 families. We analyzed the genomes, transcriptomes, and biological characteristics of iPSCs, neuronal progenitors and neurons of patients with autism spectrum disorder and macrocephaly and their unaffected family members. Using EdgeR and a generalized linear model to account for family differences we found that that probands' neuronal progenitors and neurons differ from unaffected family members with respect to biofunctions mostly related to *Cell cycle/Cell proliferation* and *Embryonic Development.* Indeed, using assays for cell proliferation and differentiation we found that cells from probands have significantly shorter cell cycle, i.e., faster cell division and increased number of proliferative neuronal precursors as compared to unaffected controls. Furthermore, these neural precursor cells derived from probands with ASD generate significantly more inhibitory GABAergic neurons, while the generation of excitatory neurons is not significantly changed.

Conclusions: These results suggest an imbalance in excitation and inhibition in early brain development in ASD. We are currently investigating whether differentially expressed genes are significantly enriched in structural and sequence DNA variation in probands. We conclude that hiPSCs can be useful as a model to elucidate the neurobiological basis of neuropsychiatric disorders of unclear etiology.

**150.004** The Influence of Pten Signaling on Brain Growth Dynamics. D. T. Page*, *The Scripps Research Institute*

Background:

In the developing brain, different cell types grow and form connections at different rates. The sum of this process is a stereotyped trajectory of brain growth that underlies the development of behavior and cognition. It is an intriguing—but largely untested—possibility that molecular and cellular regulation of this process may be a point of convergence for a subset of autism risk factors, including genes acting in the PI3K-Akt-mTOR pathway such at *PTEN.*

Objectives:

To investigate this problem, we are making use of a mouse line that carries a risk factor for autism spectrum disorder (ASD) and macrocephaly in humans, *Pten* haploinsufficiency. We are examining the developmental trajectory of brain growth in these mice, as well as the relative contributions of changes in cell number and cell size to this process, with a particular focus on the cerebral cortex. We are also testing candidate second site genetic modifiers to elucidate the

signaling network that Pten acts in to regulate the dynamics of brain growth.

Methods:

We have used a combination of immunohistochemistry, cell counting (isotropic fractionator, which allows for unbiased estimates of cell number and density in the brain) and behavioral analyses to examine the effects of *Pten* haploinsufficiency on the developmental trajectory of brain growth and ASD-relevant behavior.

Results:

*Pten* haploinsufficient mice display an accelerated brain growth phenotype that shows a dynamic pattern over development. This corresponds to changes in both cell number and size in the cerebral cortex that differentially impacts distinct cell types. We also find that *Pten* haploinsufficient mice have selective impairments in ASD-relevant behavioral tasks.

Conclusions:

These findings are a step toward understanding whether an altered trajectory of growth in the brain and constituent cell types may be a common feature across a subset of autism risk factors, and whether this may be of relevance to the behavioral and cognitive symptoms of ASD.

## 151 Active Ingredients and Therapeutic Processes in Interventions for Autism Spectrum Disorders

*Discussant:* P. J. Yoder *Vanderbilt University*

*Organizer:* M. D. Lerner *Stony Brook University*

Research on treatments for social deficits in autism spectrum disorders (ASD) has recently proliferated, leading to identification of interventions considered empirically-supported (Rogers & Vismara, 2008; Reichow & Volkmar, 2010). However, few studies have yet addressed the nuanced questions of "why and how does it work, for whom, under what conditions" (Kazdin, 2007). This has been identified as a crucial priority (e.g. Lerner, et al., 2012; Maglione et al., 2012), as identification of "active ingredients" and therapeutic mechanisms is essential to achieving the goal of optimized evidence-based therapies. There currently exist a wide array of methodological and statistical approaches to uncovering processes responsible for change in interventions. In this panel, we will introduce and describe several different approaches with unique applications to disentangling therapeutic processes across childhood. To achieve coordinated teaching across research groups, cutting edge treatment data will be used to elucidate both how given process variables relate to discrete outcomes, and what they may reflect about general process analysis principles. Key factors such as parental involvement, operative therapist behaviors, conceptual and manual fidelity, and knowledge- versus performance-training strategies will be presented, with an integrative discussion aimed at highlighting the utility and accessibility of studying therapeutic processes in ASD.

**151.001** Changes in Parental Involvement and Behavior during a Parent-Mediated Intervention for Toddlers with Autism. A. Gulsrud*[1], G. Hellemann[1] and C. Kasari[2], (1)*UCLA*, (2)*University of California Los Angeles*

**Background:** An important focus of behavioral interventions for young children with ASD is involving parents in the treatment process. Even in high intensity treatments, children with ASD are only exposed to the treatment a small portion of the overall day. By training parents in specific intervention techniques, we can increase the dose of early intervention that children with ASD receive throughout the day. While parents are believed to play a critical role in the success of these interventions, few studies have systematically examined the relationship between level of parental involvement and change in observed parental behaviors.

**Objectives:** The goal of this study was to first determine if intervention approach influences the parent's level of involvement, as well as their implementation of specific behavioral strategies in interactions with their toddlers (in this case based on JASPER, an experimental treatment that has evidence of positive child outcomes including increases in joint engagement, number of child initiated play routines, and play skills (Kasari, Gulsrud, & Hellemann, in prep)). Additionally we assessed moderating effects of parental involvement on the implementation of these strategies.

**Methods:** Eighty-six parent-child dyads participated in a randomized controlled early intervention study. Participants were randomized to either a parent-mediated JASPER condition or an individualized psychoeducational intervention (PEI) targeting parental stress-reduction (Brereton and Tongue, 2006). Families met one-on-one weekly with a trained therapist for 10 weeks. Children had an average chronological age of 31.5

months and mothers were on average 35.9 years old. The sample consisted of mostly Caucasian males with an average IQ of 68.

**Results:** This study highlights the efficacy of the parent-mediated JASPER intervention approach for parents of toddlers with ASD. Increases in therapist rated parental involvement (CIS) were larger in the JASPER group ($F(1,69)=9.85$, $p<.01$, Pre:14.6, Post:17.8)) than in the psychosocial intervention group (Pre: 15.3, Post: 15.9). Similarly, videotaped dyadic interactions, rated by coders blind to timepoint (pre or post) and randomization status, showed differences for the observed usage of environmental strategies ($F(1,81)=18.3$, $p<.01$, JASPER: .71 to .89, PEI: .70 to .73), prompting ($F(1,81)=12.1$, $p<.01$, JASPER: .48 to .69, PEI: .47 to .50), communication ($F(1,81)=14.4$, $p<.01$, JASPER:.49 to .72, PEI: .47 to 51) and imitation ($F(1,81)=10.6$, $p<.01$, JASPER: .32 to .67; PEI (.30 to .39). While there were no significant relationships between strategy use and involvement in the PEI group (all correlations <.15, all p-levels >.20), there was evidence suggesting that parental involvement in the JASPER group was specifically associated with the use of communication strategies ($r=.41$, $p=.01$) and marginally associated with the use of environment strategies ($r=.29$, $p=.08$). Methods for conducting these analyses will be reviewed.

**Conclusions:** These data suggest that a brief parent-mediated intervention can improve therapist-rated parental involvement and independently coded use of specific JASPER intervention strategies. In addition, this study suggests that maintaining and creating parental involvement is an important facet of treatment design, suggesting that child-centered interventions may also need to pay increased attention to parent involvement.

**151.002** Towards understanding the active ingredients of parent-mediated social communication interventions for young children with ASD. B. Ingersoll*, *Michigan State University*

**Background:** One approach to teaching social communication to young children with ASD has been the use of parent–mediated interventions. These interventions typically teach parents to use naturalistic intervention techniques to promote their child's social communication skills during play and other daily routines. A number of such interventions have been developed and there is growing evidence that they lead to improvement in children's social communication development. However, the active ingredients of many of these interventions have not yet been identified or systematically evaluated. A better understanding of the active ingredients of promising parent-mediated interventions is needed, especially as these interventions are moved into community settings.

**Objectives:** The goal of this presentation is to discuss what is currently known and not yet known regarding the active ingredients of parent-mediated social communication interventions for young children with ASD. In addition to a review of current work in the field, we will present data from a series of single-case design (SCD) studies that aim to illuminate the active ingredients of a parent-mediated intervention model during its development and initial evaluation phase.

**Methods:** Intervention techniques were chosen based on prior efficacy studies and combined into a parent training model that could be implemented in community settings. A series of SCD studies were used to examine the effect of the intervention on child language. To understand the efficacy of the intervention package, a multiple-baseline SCD study was used across 9 children and trained therapists. An alternating-treatments SCD was then used to systematically examine the relative contributions of individual treatment techniques from the intervention package on child language. Finally, a multiple-baseline SCD was used to examine the effect of the parent training model on parent fidelity and child language. Multilevel modeling was used to examine the association between parents' use of individual intervention strategies and their child's language use.

**Results:** Across studies, there was evidence for the efficacy of the program for improving child expressive language. In addition, several active ingredients of the intervention were identified. Specifically, parents' use of responsiveness-based strategies (following the child's lead and imitating the child) and prompting and reinforcement strategies within child-directed activities were found to be related to improvements in child expressive language within the session, while another set of techniques, modeling and expanding language, was not. Direct instruction in the intervention techniques was related to

parent fidelity; although, the frequency of instruction (once vs. twice per week) did not affect parent learning.

**Conclusions:** The results provide preliminary support for the efficacy of key components of a parent training program that can be feasibly implemented in community settings, and identify the active ingredients of the intervention (responsiveness-based strategies, language prompting). Similar approaches can be taken with other parent-mediated approaches to better understand *how* they are working and to facilitate implementation in community settings.

**151.003** Assessment of Fidelity in a Summer Program for Social Competency in Youth with ASD. J. Mendelson*[1], M. Tudor[2] and M. D. Lerner[2], (1)*University of North Carolina - Greensboro*, (2)*Stony Brook University*

**Background:** Although social skills interventions (SSIs) have recently been deemed evidenced-based for children with ASD (Reichow & Volkmar, 2010), the mechanisms of effectiveness remain unclear. Treatment fidelity (or adherence to principles and procedures of an intervention) is a common treatment mechanism in youth therapies (Perepletchikova & Kazdin, 2005); while it may be crucial in the study of ASD treatments (Wainer & Ingersoll, 2013), it is rarely examined in relation to outcomes. While multifaceted, fidelity in such interventions can generally be conceptualized as engagement manualized activities (manual fidelity) or adherence to treatment principles (conceptual fidelity; Lerner & Mikami, 2012). Given that friendship-making is a key SSI goal (Kasari et al., 2012), and recent evidence that within-group friendships may be amenable to intervention in some SSIs (e.g., Socio-Dramatic Affective Relational Intervention; SDARI; Lerner & Mikami, 2012), examination of distinct predictive roles of fidelity components, is crucial to understanding its role in SSI efficacy. Likewise, study of fidelity measurement *timing* (i.e. early in treatment versus over time) is clinically valuable for knowing when fidelity may best be addressed.

**Objectives**: 1) To demonstrate analysis of manual and conceptual fidelity in predicting outcomes in SDARI. 2) To assess relative role of early fidelity and fidelity change in predicting outcomes.

**Methods**: Thirty-four youth (9 – 16 years; 23 male) participated in 6-week summer SDARI. They completed blinded sociometric ratings of peers in their group (Coie, Dodge, & Coppotelli, 1982) after the first (early) and last (endpoint) week. Group counselors completed measures of SDARI manual and conceptual fidelity (Lerner & Mikami, 2012) twice/week. Early fidelity was calculated by averaging the two initial sessions; fidelity change was calculated via Empirical Bayes residual of fidelity over time.

**Results**: Hierarchical Linear Modeling was used to control for nesting within groups, with early and change in manual and conceptual fidelity predicting change in sociometrics. Early ($\beta_{04}$ = 1.89, $p < .05$) and increased ($\beta_{02}$ = 90.58, $p < .05$) manual fidelity predicted increased reciprocated friendships; meanwhile, *decreased* conceptual fidelity predicted increased reciprocated friendships ($\beta_{01}$ = -13.64, $p < .05$). Early manual fidelity predicted increased social preference ($\beta_{04}$ = 1.89, $p < .05$). Methods for these analyses will be presented.

**Conclusions**: Findings suggest that manual fidelity was most effective for friendship formation. Higher early manual fidelity and increased manual fidelity predicted increased reciprocated friendships, indicating that activity adherence could beneficially be promoted throughout SDARI. Results also suggest that children with ASD may benefit from a manualized structure. Higher early manual fidelity also predicted increased social preference, suggesting that content of introductory sessions may have been beneficial for within-group liking. Contrary to hypotheses, decreased conceptual fidelity predicted increased reciprocated friendships, suggesting that decreased adherence to the concepts of SDARI by counselors may have facilitated friendship-making with peers. For instance, counselors may have observed children begin to demonstrate friendship gains, and then may have taken a more passive approach to sessions over time. Results speak to the importance of further investigation into the role of fidelity throughout the course of SSIs.

**151.004** Immediate Impact and Individual Differences: Using a "Micro-Dismantling" Approach to Elucidate Dissociable Effects of Knowledge- and Performance-Training Components. M. D. Lerner*[1] and A. Y. Mikami[2], (1)*Stony Brook University*, (2)*University of British Columbia*

**Background**: While social skills interventions (SSIs) for ASD have been deemed "evidence-

supported" (Reichow & Volkmar, 2010), little work has explored common components of SSIs that may be responsible for outcomes, such as social knowledge (SK) training (didactically teaching appropriate behaviors) and social performance (SP) training (providing opportunities for engagement in prosocial behaviors, regardless of knowledge; Gresham, 1997). One approach to doing so is "dismantling," where individuals are randomized to specific elements of treatment packages to identify "active ingredients" (Kiesler, 2004). A small study using this approach identified differences in peer engagement after a single session of SK- and SP-training, suggesting that effects on social behavior occur quickly (Lerner & Mikami, 2012). Thus, further exploration of immediate, component-specific mechanisms is plausible via brief "micro-intervention" sessions (Holtforth et al., 2004). Likewise, by considering individual differences in baseline abilities, such a design can be used to identify "aptitude x treatment" (AxT) effects (Smith & Sechrest, 1991), which can answer crucial questions of *how* and *for whom*a treatment component may work (Kazdin, 2007).

**Objectives**: 1) To demonstrate the use and analysis of a "micro-dismantling" study to identify differences in effects of SK- and SP-training on peer engagement. 2) To elucidate AxT effects in SK- and SP-training.

**Methods**: Thirty-eight youth with confirmed ASD (30 male; $M_{age}$ =12.92, $SD_{age}$= 2.09) completed a lab-based session in which they were randomly assigned, in dyads of previously-unacquainted participants, to complete 20 minutes of SK- or SP-training. Participants engaged in 10 minutes of free interaction immediately pre- and post-training. Peer engagement during training and free interaction was taped and coded by blinded, reliable coders for total and positive interaction (Bauminger, 2002). Participants completed baseline diagnostic (Lord et al., 2002), IQ (Wechsler, 2004), explicit SK (Michelson & Wood, 1982), and SP-linked (efficiency of processing social information, indexed by N170 ERP latency [Lerner et al., 2013]) measures.

**Results**: Generalized Estimating Equations with ANCOVA-of-change models (controlling for diagnostic and IQ scores) were used to account for nesting within dyads and estimate change in peer interaction. Analysis methods will be presented. Participants showed relative increases in total ($B$ = .67; $p$ < .001) and positive ($B$ = .58; $p$ < .001) peer interaction during SP- versus SK-training. For AxT, faster N170 predicted increased interaction regardless of condition ($B$ = -.06, $p$ = .021), but greater increases in positive interaction in SP-training ($B$ = -.24, $p$ = .043). Higher levels of social knowledge ($B$ = -.04, $p$= .001) predicted greater increases in positive interaction during SK- versus SP-training.

**Conclusions**: The "dismantling" approach revealed relatively greater increases in positive peer interaction during SP-training, suggesting that theorized "opportunities for engagement" are uniquely presented in this component. The AxT analyses suggested that youth with faster N170s may capitalize more on positive interactions, but that they may be uniquely able to capitalize on SP-training to achieve richer peer interaction. Conversely, those with greater SK appear to benefit from didactic interaction training, suggesting it may act as a "learning style" in some youth with ASD.

## 152 Drug Development in Autism Spectrum Disorder

*Discussant:* B. King *University of Washington & Seattle Children's Hospital*

*Organizer:* L. Scahill *Marcus Institute, Emory University*

Two medications, risperidone and aripiprazole, are approved by the US Food and Drug Administration for the treatment of irritability in children age 5 to 17 with DSM-IV autistic disorder. There are no approved medications for social disability or repetitive behavior in autism specifically or autism spectrum disorder (ASD) more broadly. Over the past decade several genes have been identified that dramatically increase the risk of ASD. Identified genes include those causing monogenic disorders (e.g., Fragile X, neurofibromatosis), as well as rare mutations and de novo mutations. These genetic abnormalities may affect the structure and function of neurotransmitter receptors, the intracellular function of neurons, development of neural networks and signaling between neurons among other neurobiological functions. As more is learned about the function of the genes that contribute to the etiology of autism, there is expanding potential for drug development. This scientific panel will present a series of talks outlining the central issues facing drug development in ASD: the role of pilot studies, compound selection, the importance of biomarkers and ethical considerations for studies involving developmentally disabled individuals.

**152.001** Place of Pilot Trials in Drug Development for ASD. L. Scahill*, *Marcus Institute, Emory University*

Background: Large-scale, NIMH-funded, multisite trials in ASD take time (three to five years) and money (5 to 10 million dollars depending on the sample size and length of trial). If we are to use resources wisely, the selection of compounds for large-scale study warrants careful consideration.

Objectives: The purpose of this presentation is to describe the role of pilot studies in drug development. The discussion will also highlight the research questions that pilot studies are not equipped to answer.

Methods: We surveyed published literature over the past decade to identify the aims and findings of selected pilot studies in ASD. We also reviewed seminal papers by experts on the appropriate use of pilot studies in drug development.

Results: Pilot trials paly an essential role in drug development by providing information on drug mechanism, drug dosing, time to clinical effect, adverse effects and acceptability in the ASD community. For example, in the absence of hype (secretin), new compounds with no prior use in in ASD may be greeted with skepticism in the autism community. Assumptions about the drug mechanism may result in narrow entry criteria that may hinder or even halt enrollment. On the other hand, pilot trials focused on mechanism should avoid overly broad entry criteria, which could result in a heterogeneous sample and a poor test of the mechanism. Dosing strategies adopted from another clinical population may not be tolerated in ASD resulting in attrition. That subjects with ASD do not tolerate medications as well as other clinical populations argues in favor of flexible rather than fixed-dose strategies. The presentation will show that information on acceptability, tolerability and treatment compliance is more useful than information on efficacy in pilot trials. Indeed, focus on efficacy in pilot studies inevitably faces the possibility of false positive and false negative findings. Over-interpretation of false positive findings may lead to unnecessary expenditure of resources on compounds that do not warrant further study. Premature acceptance of negative findings from a pilot study may lead to rejection of a potentially useful drug. The presentation will also provide examples of useful pilot trial designs.

Conclusions:

The role of pilot studies is to assist with the critical judgment on whether a given compound warrants further study. Pilot trials are not about efficacy and not about estimating effect size for a larger clinical trial.

**152.002** Hot Targets for Compound Selection in ASD Trials: The NIMH FAST-ASD Network. J. T. McCracken*, *UCLA Semel Institute for Neuroscience & Human Behavior*

Background: Pharmacological clinical trials in autism spectrum disorder (ASD) aiming to change core domains have yielded disappointing efficacy results. Although progress in basic science, ASD animal models, and genetics in ASD has been substantial over the past decade, the identification of compelling targets for ASD clinical trials has been a challenge and early targeted therapies have fallen short. There are several likely reasons for these failures, including inadequate integration of basic science knowledge with available, although incomplete, clinical findings, ill-defined subject selection and incomplete matching of the primary outcome measure with the chosen target (e.g., social communication).

Objectives: The aim of this presentation is to describe an approach to target selection driven by an effort to integrate basic and clinical findings to identify specific candidate compounds for early clinical trials in ASD.

Methods: Based on literature review, the presentation will provide selected examples of compounds with mechanisms of action that may be relevant to ASD.

Results: There are a number of promising targets for investigation in ASD, some with strong evidence implicating their relevance to core domains of the ASD phenotype. After discussing the model for target selection, the presentation will describe the approach taken by the recently launched NIMH-initiated "Fast Fail Trials in Autism Spectrum Disorders (FAST-AS)." This initiative is designed to identify and rank order promising compounds for ASD to set a course for drug development in ASD. The GABA system emerges as a compelling target with links to core and associated features of ASD. Thus, the compound selection process will be illustrated by reviewing a highly ranked target in the GABA system. Aspects

of trial design related to this approach will also be discussed.

Conclusions:

We are in an era of rapidly emerging findings from many sources on the pathophysiology of ASD. To make use of this accumulating information in basic science, biomarkers and clinical measurement, we need to modify our approach to drug selection, early study designs to advance drug development in ASD.

**152.003** How Can Biomarkers Enhance Clinical Trials in Autism Spectrum Disorder?. M. Grabb*, *National Institute of Mental Health*

Background: Pharmacological clinical trials in autism spectrum disorder(ASD) have yielded mixed results in efficacy. One challenge that may contribute to this situation is the heterogeneity in study participants, lack of biological targets associated with deficits in the core domains of ASD dysfunction, and the lack of objective biological measures of treatment response.

Objectives: The goal of this presentation is to discuss the promise of biomarkers in stratifying subjects to enrich for the specific deficit being tested in the trial, and to highlight outcome measures that may inform whether a treatment is working.

Methods: NIMH has created a program, called the "Fast Fail Trials" which is designed to develop and test ASD biomarkers in clinical trials of investigational compounds. Before initiating the first trial, we formed an advisory committee to establish compound selection criteria, identify compounds to test and then help inform the biomarker selection.

Results: There is a wide range of biomarkers that are being tested in ASD but much fewer being incorporated into trial designs. Examples of potential biomarkers include brain activity measures such as fMRI and EEG/MEG, peripheral measures that correlate with sympathetic nervous system activity, eye tracking, various cognitive assessments, actigraphy, sleep measures and peripheral blood measures. This presentation will provide an overview of different biomarkers being studied in ASD that could be used in stratifying subjects and/or assessing treatment response. The significant effort needed to incorporate biomarkers in ASD trials will be emphasized. To illustrate how this can be done, the presentation will provide 1-2 case examples on the application of biomarkers into an ASD trial, based on NIMH's recent efforts in the Fast Fail Program

Conclusions:

Different methodologies are becoming available to test how biomarkers can be used to stratify or enrich for subjects with specific phenotypes (deficits in a core domain of function) in ASD clinical trials. However, many studies have used small numbers of subjects and broad inclusion criteria and therefore the measures have not been tested or validated for their ability to define subgroups with ASD that may benefit most from the intervention. Challenges remain as to the feasibility, specificity (developmental age, level of function, core symptom), reproducibility, sensitivity of measures to change over time, etc. Especially in early treatment trials, the ability to correlate a brain activity measure such as EEG or fMRI with cognitive outcomes may be more informative than reliance on behavioral measures or patient reported outcome measures. The timing is right to begin incorporating quantitative biological measures into trials to test novel hypotheses for therapeutic interventions.

**152.004** Ethical Dilemmas in Drug Development in ASD. L. Politte*, *Lurie Center*

Background: Developing new drugs for the core features of autism spectrum disorder (ASD) will involve compounds that are not commercially available. Although ASD begins in early childhood, the regulatory pathway for drug approval usually starts with healthy (unaffected) adults, followed by adults with the disorder of interest, then advancing to pediatric trials.

Objectives: The purpose of this presentation is to describe the ethical issues confronting drug development in ASD with particular focus on the inclusion of subjects with intellectual disability.

Methods: We reviewed available literature to identify the web of ethical issues inherent in drug development programs for ASD.

Results: First, we note that approximately half of the ASD population has an additional diagnosis of intellectual disability (ID). A history of past unethical research and clinical practices involving

individuals with ID has prompted calls for additional protection of individuals with ID who participate in clinical research. This appropriate concern about exploitation of a vulnerable population, however, must be balanced with the problem of excluding these subjects from research with the potential of benefit. Therapeutic benefit observed in studies including only higher-functioning participants with ASD may not generalize to individuals with ASD and ID. Furthermore, individuals with ASD and ID are more likely to have serious behavioral problems, such as self-injurious behavior, that are often refractory to current drug treatments and may benefit from novel approaches. A second ethical dilemma arises from the fact that early clinical drug trials may focus on drug mechanism and may not provide direct benefit to individual subjects. Confirmation of the drug mechanism may be an important step in drug development and may result in societal benefit. However, subjects who benefit from treatment in an early drug trial may not have access to the drug after the trial due to uncertainty about long-term effects of new compounds. Although benefit to society is an acceptable rationale for proceeding with studies that do not provide direct benefit to participants, the hard fact that the drug will not be available - even if it helps - may be a difficult concept to communicate to developmentally disabled participants. At the same time, societal benefit may be reduced if subjects with ID are not included in trials of drugs from which they may benefit.

Conclusions: Drug development in ASD should include subjects across the full range of intellectual functioning. Critical discussions are needed to work through concerns of exploitation and exclusion of subjects in need of new treatments.

## 153 Adult Outcome: Medical, Cognitive, Behavioral

**153.001 1** Adjustment to University and the Broad Autism Phenotype. D. A. Trevisan* and E. Birmingham, *Simon Fraser University*

Background:

As more and more individuals with ASD enter university, it is vital for educators to understand how best to support these students (VanBergeijk et al., 2008). In addition, many university students, while not clinically impaired, are likely to exhibit traits associated with the Broad Autism Phenotype (BAP; Hurley et al., 2007). Given that BAP traits in the general population are associated with poorer social cognitive and communication skills (Sasson et al., 2012), BAP traits in the general student body may serve as powerful predictors of adjustment to the social and academic demands of university life.

Objectives:

The purpose of this study was to investigate possible relationships between student adjustment to university and the BAP. Examining the relationship between autistic traits and university adjustment will provide valuable information that could aid universities in designing interventions used to promote adjustment to university, thereby improving the likelihood of retaining students to degree completion.

Methods:

Data from 92 undergraduate students from a university in Western Canada were analyzed. BAP traits are measured using Hurley et al.'s (2007) self-report Broad Autism Phenotype Questionnaire (BAPQ). The BAPQ was separated into three subscales: *Pragmatic language difficulties (BAPQ-Pragmatic*), *Social abnormalities and aloof personality* (*BAPQ-Aloof*), and *Rigid personality and a desire for sameness* (*BAPQ-Rigid*). University adjustment was measured using the self-report Student Adaptation to College Questionnaire (SACQ; Baker & Siryk, 1999). We analyzed three subscales including *Social Adjustment*, *Personal-Emotional Adjustment,* and *Academic Adjustment*.

Results:

Multiple regression was performed on each subscale of the SACQ separately (entering the three BAPQ subscales as predictors). This analysis revealed that pragmatic language difficulty was the strongest predictor of student adjustment, emerging as a significant predictor for each SACQ subscale (social: b = -0.37; personal-emotional: b = -0.36; academic: -0.43 *p*s < 0.01): higher *BAPQ-Pragmatic* scores were associated with poorer social ($r$ = -0.52), personal-emotional ($r$ = -0.49), and academic ($r$ = -0.51) adjustment to university. Rigid personality traits also emerged as a significant predictor, but only for personal-

emotional adjustment (b = -0.30, p<.01), with higher *BAPQ-Rigid* scores associated with poorer personal-emotional adjustment (*r* = -0.43). Finally, the aloof personality trait was a significant predictor of social adjustment (b = -0.35, p<.001), with higher *BAPQ-Aloof* scores associated with poorer social adjustment *(r* = -0.50*).* Together, *BAPQ-Pragmatic* and *BAPQ-Rigid* accounted for 32% of the variance in personal-emotional adjustment ($R^2$=0.32; F(2,87) = 20.21, *p*<.001). *BAPQ-Pragmatic* and *BAPQ-Aloof* accounted for approximately 37% of the variance in social adjustment ($R^2$=0.37; F(2,86) = 25.24, *p*<.001). Only *BAPQ-Pragmatic* predicted academic adjustment, accounting for approximately 25% of the variance ($R^2$=0.25; F(2,89) = 29.42).

Conclusions:

Autistic traits in the university student body accounted for a significant amount of variance in student adjustment. Pragmatic language difficulties, in particular, emerged as a strong predictor of social, personal-emotional, as well as academic adjustment. These results have two broad implications: (1) to promote student adjustment, universities should consider utilizing interventions that aim to enhance students' social communication skills; (2) the BAPQ might be a useful screening measure to predict potential adjustment difficulties among incoming students.

**153.002 2** Disconnected Postsecondary Youth with ASD: What Are They Doing? What Do They Need?. P. Shattuck*, *A.J. Drexel Autism Institute, Drexel University*

Background: Recent work has documented that 35% of youth with ASD have no participation in any vocational education, college, or paid employment of any kind during the first seven years after exiting high school (Shattuck, et. al, 2012). This rate of disconnection is over 50% in the first two years after high school. A life course perspective suggests that the transitional period of development from adolescence to young adulthood is an especially important period. A positive set of experiences can provide a solid foundation for successful social functioning into later adulthood. A negative set of experiences can increase the risk for poor developmental, health, and social outcomes.

Objectives: This poster aims to answer the following questions about the youth who are disconnected in the years immediately after high school. Are they receiving vocational services? Are they participating in community life some other way, perhaps in a day habilitation program? What other services are they receiving? What percentage of families report a need for vocational and life skills services (potential stepping stones to connection with school or work)?

Methods: Data come from the National Longitudinal Transition Study-2 (NLTS2). The study was conducted over 5 waves, 2 years apart, from 2001 to 2009. At baseline, all youth were ages 13 – 16 years old and receiving special education services. The study began with over 11,000 students, including 920 in the autism special education category. Estimates for this poster come from Wave 5 conducted in 2009, when youth were in their early- to mid-20's, and are weighted to be nationally representative of the cohort of youth served in the autism special education category at the start of the study.

Results: Of those not engaged in education or paid work at any point since exiting high school, 15% had never received any vocational support services and 30% had no participation in other community activities such as a day habilitation program. Just over one quarter had never received any of the following supportive services since exiting high school: vocational services, life skills instruction, mental health intervention, transportation assistance, day habilitation, personal assistant, speech therapy, or case management. One third of families expressed a need for vocational services and just over one half expressed need for life skills training.

Conclusions: Youth with an ASD are at a particularly high risk for a period of struggling to find ways to participate in work and school after leaving high school. A large proportion of these disconnected youth are also not involved in any other supportive services or activities that might be considered stepping stones to productive community participation. This study suggests there are significant lapses in transition planning for youth with autism. Future research should examine how to improve transition planning and the process of connecting youth with postsecondary opportunities upon exiting high school.

**153.003 3** Examining Vocational Services for Adults with Autism. D. B. Nicholas*[1], L. Zwaigenbaum[2], M. Clarke[1], K. P. Stoddart[3],

P. Mirenda[4], I. M. Smith[5], C. Carroll[6], W. Roberts[7], B. Muskat[8], M. Spoelstra[9], T. Jackman[10], S. Duhaime[3], H. Emery[1], L. Ghali[11], D. Barrett[12] and L. Parakin[13], (1)*University of Calgary*, (2)*University of Alberta*, (3)*The Redpath Centre*, (4)*University of British Columbia*, (5)*Dalhousie University / IWK Health Centre*, (6)*Autism Nova Scotia*, (7)*University of Toronto*, (8)*The Hospital for Sick Children*, (9)*Autism Ontario*, (10)*Autism Society Canada/Autism Society Newfoundland and Labrador*, (11)*The Ability Hub*, (12)*Autism Society of Edmonton Area*, (13)*Autism Calgary Association*

Background: N/A

Objectives:

The Canadian unemployment rate for persons with disabilities including ASD, is estimated at 53.2% (HRSDC, 2009) compared to 7.9% in the general population (Statistics Canada, 2010). Addressing this unacceptably low employment rate, we examined types of vocational services offered to adults with ASD, perceptions of vocational service quality, and related experiences of adults with ASD, caregivers, employers, and employment support personnel, regarding vocational services in ASD.

Methods:

A mixed method design incorporated the following: (i) a web-based environmental scan based on a website review of international ASD vocational resources, (ii) a survey eliciting vocational models in ASD, (iii) in-person interviews with adults with ASD and family members examining vocation-related experiences and needs of adults with ASD; and (iv) interviews with supported employment personnel and employers addressing employment support personnel and employer perceptions and needs in establishing sustained work placements for adults with ASD.

Results:

A total of n=126 senior personnel from Canadian employment support agencies were surveyed. Interviews and focus groups were subsequently conducted with 188 participants, including individuals with ASD (n=51), family members or other formal/informal caregivers (n=71), employers (n=22), and vocational service providers (n=44). Environmental scan, survey and interview data suggest a range of models comprising community programs, pre-employment (job findings) training, job skills training, life skills facilitation, job coaching, and on site training, using various methodologies including technology-based applications. Participants consistently report insufficient opportunities and supports for persons with ASD in the workplace. In terms of agency survey results, findings suggest that service agency personnel are generally satisfied with the vocational support offered within their agency given the resources they have available. However, the majority of respondents indicate dissatisfaction with the availability of vocational support resources within their region. Qualitative interview findings identify the following themes: having an ASD diagnosis can serve as both a challenge and a blessing in seeking employment; negative attitudes towards the inclusion of persons with disability impact vocational experience; positive or negative employment experiences have a corresponding impact on employees' confidence in subsequent vocational pursuits; substantial difficulties are encountered in transition to adult resources; and workplace cultural shifts can enhance the vocational experience of individuals with ASD. Participants identified inconsistencies between the aims of support resources versus the actual experiences and needs of individuals with ASD and their families. Generally, support program impact was perceived more favorably by employment support personnel than by the recipients of these services. There is a frequent lack of opportunity for vocational placement, and participants report a lack of protracted support to facilitate employment retention. Participants call for a person-centred, targeted and seamless approach to vocational support. More engagement with employers in building capacity is strongly recommended.

Conclusions:

Greater employment access is needed, as are models, capacity-building tools, and evaluation metrics to guide vocational support practices. Practice, research and policy implications will be offered. This includes advocacy and action at multiple levels including support resource development for the individual with ASD (employer) and family as well as the vocational support personnel and employer.

**153.004 4** Five Factor Personality and Adults with Autism. B. Schwartzman*[1], J. J. Wood[2] and S. K. Kapp[3], (1)*UCLA*, (2)*University of California Los Angeles*, (3)*University of California, Los Angeles*

Background: Adults with autism, regardless of level of functioning, demonstrate generally poor prognoses. Research suggests studying the personalities of individuals with autism could give better insight into the heterogeneity that exists within the autism phenotype (Eaves et al., 1994; Hepburn & Stone, 2006; Ozonoff et al., 2005; Schwartz et al., 2009; Wing, 1997). Based on extensive research from a variety of cultures and age groups, there is a well-established consensus among personality researchers that the Five Factor Model of Personality ("The Big 5") provides a robust account of the dimensions of human personality variation and behavior. To date, very little is known about the personality traits associated with Autism Spectrum Disorders, and even less is known regarding how individuals with autism present in terms of the Five Factor Model of Personality specifically (Ozonoff et al., 2005, De Pauw et al., 2011).

Objectives: (1) To determine the extent to which The Big 5 and its facets account for variability in Autism Spectrum Disorder (ASD) symptomatology in adults with and without diagnoses of ASD (2) To verify differences in personalities of adults with and without ASD at both the factor and facet-levels and (3) to empirically identify distinct behavioral phenotypes that exist within ASD in terms of Big 5 factors and facet-level variability.

Methods: A sample of 821 adults (359 with ASD; 462 without) completed an online survey consisting of the Ritvo Autism Asperger's Diagnostic Scale Revised (RAADS-R; Ritvo et al., 2010), the International Personality Item Pool Representation of the NEO-PI-R (IPIP-NEO-120; http://ipip.ori.org), and demographic information. The RAADS-R is an 80-item self-rated diagnostic scale for measuring autism based on the DSM-IV and ICD-10 diagnostic criteria. The IPIP-NEO-120 is an online, public domain tool for personality measurement which reports the individual level of personality under each of the five domains in the Five-Factor Model.

Results: IPIP-NEO-120 scores accounted for 71% of the variance in RAADS-R scores. Neuroticism was found to be positively correlated with RAADS-R scores, while Extraversion, Openness to experience, Agreeableness, and Conscientiousness were found to be negatively correlated with RAADS-R scores. Based on *k-means* Cluster Analysis, four distinct Big 5 personality subtypes emerged within adults with ASD.

Conclusions: Information gained from this study further emphasizes the "spectrum" nature of autism, in that an autism diagnosis consists of a variety of behaviors and symptoms that manifest differently from person to person. Results indicated that while the personalities of adults with and without autism significantly differed as expected, personality differences also emerged within the group of adults with autism. These findings provide direction for future intervention, by describing individuals on the autism spectrum based on a continuum of combinations of personality factors, a true spectrum, as opposed to characterizing these individuals solely based on being "low" or "high" functioning.

**153.005 5** A Pilot RCT for Adults with ASD: The Interview Skills Curriculum. L. Morgan*[1], A. Leatzow[1] and M. Siller[2], (1)*Florida State University Autism Institute*, (2)*Hunter College of the City University of New York*

**Background:** Outcomes for adults with ASD indicate low rates of competitive employment, independent living, and friendships; even for those with normal IQ (Howlin et al., 2004). Social-pragmatic deficits are a significant source of impairment for individuals with ASD regardless of cognitive or language ability (Carter et al., 2005) and may serve as a critical target area to improving adult outcomes. This submission presents data from a pilot RCT to test the effects of a job interview skills curriculum for adults with ASD funded by Autism Speaks.

**Objectives:** The purpose of this study was to evaluate the effects of the *Interview Skills Curriculum'* for young adults with ASD. We hypothesized that adults who receive ISC would show significant gains in targeted social and pragmatic skills between baseline and 6-month follow up.

**Methods:** Twenty-eight adults diagnosed with ASD were recruited to participate in this research. Participants ranged in age from 18 to 36 years (M = 24.5, SD = 5.2), scored above 70 on an abbreviated test of intelligence (M = 103.0, SD = 14.7), but showed significant deficits on the Vineland Adaptive Behavior Composite (M = 77.4,

SD = 11.6). Pairs of participants were matched on cognitive level and randomly assigned to one of two groups: ISC or waitlist control. ISC is a manualized 12-week, low-intensity group-delivered intervention aimed at increasing social-pragmatic skills essential to the context of the job interview. Mock job interviews conducted pre- and post-treatment served as the primary source of data collection. Volunteer professionals unknown to the research participants conducted video-recorded mock interviews with scripted questions tailored to match participant career interests. Interviews were scored by a trained undergraduate coder blind to group assignment and interview timing. Inter-observer reliability was calculated for approximately 20% of the data yielding an average percent agreement of 92.6%

**Results:** Preliminary analyses (i.e., independent-samples t-tests; Chi-square tests) confirmed that the experimental and control groups were not different at baseline in terms of age, ADOS total scores, the Vineland Adaptive Behavior Composite, IQ scores, performance during the mock interview, or participants' educational attainment, ($p > .50$). In addition, key analyses were conducted to evaluate the effect of ISC on gains in the participants' observed performance during the mock interview. Consistent with recommendations for clinical trials (Fitzmaurice et al., 2004), gains in performance scores were quantified as residual gain scores. Results revealed that the experimental group showed larger gains in mock interview performance than the control group, $t(22) = 2.14$, $p < .05$ (large effect size, Glass's delta = .87). In the experimental condition, mean performance scores increased from 18.75 (SD = 3.6) to 20.75 (SD = 2.8) between pre and post assessments, while the scores in the control condition remained unchanged, 18.79 (SD = 2.55) and 18.83 (3.12), respectively.

**Conclusions:** The results of this study indicate that a brief, low-intensity treatment can significantly improve the social-pragmatic skills critical to a successful job interview for young adults with ASD. These findings will be discussed in terms of clinical implications and future research directions.

**153.006 6** Psychosocial Outcomes of a Community Sample of High Functioning Individuals with Autism Spectrum Disorder. B. D'Entremont*[1], S. Nichols[2], S. Byers[1] and S. Voyer[1],

(1)*University of New Brunswick*, (2)*ASPIRE Center for Learning and Development*

**Background:** Individuals with high functioning Autism Spectrum Disorder (HF-ASD) are reportedly not reaching their potential in terms of psychosocial outcomes (Howlin, Goode, Hutton & Rutter, 2004; Levy & Perry, 2011). However, the use of select clinical samples limits our ability to generalize findings to the broader group of individuals with HF-ASD in the community. One study suggests there is a large cohort of adults in the community, who are undiagnosed yet meet diagnostic criteria for ASD, who are as impaired in terms of psychosocial outcomes as those with a formal diagnosis (Stuart-Hamilton & Morgan, 2011); however, little is known about this undiagnosed group. Moreover, there is a lack of information on age trends in adulthood, including a scarcity of information on older adults and on gender differences within this population.

**Objectives:** To examine the effects of age, gender and professional diagnosis on ASD symptoms and psychosocial outcomes of a large sample of adults with HF-ASD purposefully recruited from the community. Four research questions were investigated: 1) do ASD symptoms and psychosocial outcomes improve across adulthood; 2) do men and women differ in their ASD symptoms and psychosocial outcomes; 3) do ASD symptoms and psychosocial outcomes differ between individuals who do and do not have a formal diagnosis; and 4) do these latter two factors interact with age?

**Methods:** Participants were 397 individuals (160 male, 237 female; age range 21 – 73 years) with HF-ASD who met cut-off criteria on the Autism Spectrum Quotient (AQ), a brief screening questionnaire designed to measure degree of ASD symptomatology in adults (Baron-Cohen et al., 2001). Participants completed online questionnaires regarding ASD symptomatology and psychosocial functioning including education, adaptive skills, employment, living arrangements, relationships and parental status.

**Results:** Participants in their 20s tended to report completing high school or less. Older participants reported completing college or undergraduate education ($F_{(3,380)} = 7.61$). Participants in their 20s reported being able to complete adaptive skills independently a little more than "sometimes". Participants in their 50's

reported completing skills independently "most of the time" ($F_{(3,381)}$ = 3.57, $p$ = .01). Older people were more likely to have been in a relationship (*Chi-square*$_{(3)}$ = 38.69, $p$ = .00) and to have children (*Chi-square*$_{(3)}$ = 71.10 , $p$ = .00). Men were more likely to be employed full-time (*Chi-square*$_{(3)}$ = 19.56 , $p$ = .00) and women were more likely to have been in a long-term relationship (*Chi-square*$_{(1)}$ = 22.80 , $p$ = .00). Finally, people with a professional diagnosis had significantly higher AQ scores ($F_{(1,381)}$ = 5.86, $p$ = .02), however this difference was not clinically meaningful ($m$ = 40 vs. $m$= 39).

**Conclusions:** People with HF-ASD continue to further their education and to acquire skills throughout their adult years. In keeping with the general population, people with HF-ASD seem to be entering into relationships and having children in their 30's. Few gender differences were found. Finally, the results also suggest that people without a formal diagnosis are functioning at a level similar to those with a formal diagnosis.

**153.007 7** The Relationship Between Stress and Social Functioning in Adults with Autism Spectrum Disorders. L. Bishop-Fitzpatrick*[1], N. J. Minshew[2] and S. M. Eack[1], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

**Background:** Adults with autism spectrum disorder (ASD) face substantial challenges accomplishing basic tasks associated with daily living, which are exacerbated by their broad and pervasive difficulties with social interactions. These challenges put people with ASD at increased risk for psychophysiological distress, which likely factors heavily into social functioning for adults with ASD, as suggested by a growing literature on stress in children that indicates that children with ASD have differential responses to stress than healthy children. We hypothesized that adults with ASD would experience more stress than healthy controls and that there would be an inverse relationship between stress and social functioning in patients with ASD.

**Objectives:** Assess differences in stress between verbal adults with ASD and without intellectual disability (n=36) and healthy controls (n=39). Examine the relationship between stress and social functioning composite scores in verbal adults with ASD and without intellectual disability (n=36) and healthy controls (n=39).

**Methods:** Baseline data were collected from 36 adults with ASD and 39 controls who were participants in a randomized-controlled trial of Cognitive Enhancement Therapy and Enriched Supportive Therapy. Composite stress (perceived stress and interviewer-observed stress on the Brief Psychiatric Rating Scale; higher scores indicate greater stress) and social functioning (global functioning using the Global Assessment Scale and social adjustment using the Social Adjustment Scale-II; higher scores indicate better functioning) scores were used to test the hypotheses. Average age was 23.4 for patients with ASD and 26.0 for controls (p=.047). Males accounted for 88.9% (n=32) of patients with ASD and 74.4% (n=29) of controls. Mean full-scale IQ was 109.3 for patients with ASD and 105.0 for controls. Racial and ethnic minorities accounted for 22.2% (n=8) of participants with ASD and 17.9% (n=7) of controls. Analyses examined both stress levels among patients with ASD and controls and the relationship between stress and global functioning for both patients with ASD and controls, controlling for age.

**Results:** As expected, results indicated that adults with ASD both perceived themselves and were perceived as having greater stress (M=3.29) compared to controls (M=1.56), F(1,72)=228.909, p<.001, and that age significantly predicts stress in patients with ASD and controls, F(1,72)=6.822, p=.011. In adults with ASD, stress was significantly related to social functioning ($\beta$*=-.241, t(33)=-4.631, p<.001,* $sr^2$*=.352*), after controlling for age, but this was not the case with controls ($\beta$*=-.081, t(36)=.868, p=.391,* $sr^2$*=.019*). This indicates that adults with ASD with higher stress were more likely to have poorer social functioning, but that stress was not significantly related to social functioning in controls in the current sample.

**Conclusions:** Findings indicate that adults with ASD experience greater perceived and interviewer-observed stress than controls and that stress is significantly related to social functioning in adults with ASD. These findings highlight the role of psychosocial distress in determining adult functioning and outcomes in this population. Results also suggest the need to develop and assess treatments that are designed to target stress and coping in adults with ASD.

**153.008 8** Anxiety and Depression in Adults with Autism: Implications for Clinical Care and Research in India. N. Singhal*[1], T. C. Daley[2], D. Taneja[1], S. Suryanarayan[1], R. S. Brezis[3], T. Weisner[3] and M. Barua[1], (1)*Action For Autism*, (2)*Westat*, (3)*UCLA*

Background: Autism in India remains a highly stigmatized condition, and many adults with high functioning autism are likely to be undiagnosed and "hidden." Emerging evidence across the world suggests anxiety and depression are probably the most common psychiatric disorder occurring in persons with autism. However, available research on anxiety and depression has focused largely on children or adolescents. Much less has been published on adults with anxiety and depression, especially at the higher functioning end of the spectrum (Engstrom, Ekstrom, & Emilsson, 2003; Hurlbutt & Chalmers, 2004). From our clinical experience in India, we are aware that adults with Autism Spectrum Disorders (ASD) face many challenges: Barriers to meaningful work; difficulty being understood within their families; challenges related to social norms about marriage, and other related issues. Given the isolation that adults with ASD may feel, it is possible that their mental health needs are being overlooked.

Objectives: This paper provides the first assessment of anxiety and depression in a sample of high functioning adults with autism in India.

Methods: As part of a larger study on families of adults with autism, 15 interviews with completed with high functioning adults with ASD (13 males, 2 females; age range of 18-33 years) residing in New Delhi and the National Capital Region, India. Interviews lasted between 2.5-4 hours. Diagnosis was confirmed using Module 4 of the ADOS and the Social Responsive Scale (SRS-II), completed by the adults. In addition, parents also completed the SRS-II to ascertain diagnosis. Adults with autism completed the Glasgow Anxiety Scale (GAS) and Beck's Depression Inventory (BDI) in an interview format. All instruments were offered to adults in the language of their preference. During a concurrent semi-structured interview with parents, extensive information was collected through interviews regarding the adults' use of medication and interventions, daily routines, sexuality, and other related topics.

Results: All participants met the cut off criteria for ASD on the ADOS and SRS-II. Of the 13 adults with ASD who completed both the GAS and BDI, 12 participants met the cut off criteria (Mindham & Espie, 2003) for presence of anxiety and 11 adults reported at least a mild mood disturbance. Degree of depression in adults with autism was positively associated with autism symptoms on the self-report SRS-II ($p$=.005). Anxiety was negatively associated with the number of hours adults spent in a structured setting ($p$=.04). More anxious adults spent fewer hours in such settings, and a greater percentage of their time alone ($p$=.03).

Conclusions: This is the first known study from India to assess the presence of anxiety and depression in adults with ASD and suggests that the mental health needs of this population may be largely overlooked. These findings underscore the need for identification, treatment and prevention of anxiety and depression for adults with ASD as well as a need to build services and support systems for adults with autism.

**153.009 9** Neurological Examination Findings in Autistic Adults. B. K. Woodruff*[1], A. K. Duffy[1], E. Pollard[2], J. G. Hentz[1], D. E. Locke[1], Y. E. Geda[1] and C. J. Smith[3], (1)*Mayo Clinic Arizona*, (2)*SARRC*, (3)*Southwest Autism Research & Resource Center*

Background: Neurological signs have been described in the setting of childhood autism spectrum disorders (ASDs), including dyspraxia, abnormal movements and tone. The presence of neurological findings in autistic adults has been described, but is not well-characterized.

Objectives: To describe neurological examination findings in autistic adults, with an emphasis on several findings not well-described in prior reports. Correlations between neurological examination findings and performance on neuropsychological measures are also reported.

Methods: In this preliminary cross sectional study 30 autistic adults, age range 20-58 years (mean age +/- SD; 31 +/- 13 years), 73% men, with

educational level (mean +/- SD) 13.4 +/- 2.1 years (range 10-18 years), underwent standard neurological examinations to identify any atypical findings.

Results: Neurological exam findings were divided into two categories, those traditionally associated with autism (97%), which included repetitive movements (33%), atypical gaze (50%), and atypical speech/language (57%); and other exam findings (83%) which included atypical gait (30%), tremor (30%), autonomic features (33%), and atypical hand posturing during gait assessment or with postural maintenance (40%). Atypical hand posturing more commonly occurred in subjects with traditional repetitive movements (p=.004). Presence of repetitive movements was inversely associated with total learning and long delay recall on the Rey Auditory Verbal Learning Test (AVLT), Delis-Kaplan (D-K) Letter Fluency and WAIS Full Scale IQ scores. Presence of atypical speech demonstrated a similar inverse association with AVLT total learning and delayed recall as well as Boston Naming Test (BNT) performance. Atypical gaze was inversely associated with D-K Tower Test performance. Tremor was associated with better WAIS Perceptual Reasoning performance. Abnormal gait was inversely associated with performance on multiple neuropsychological measures (several D-K tests and WAIS subscales, AVLT long delay recall, Rey Complex Figure copy and recall, BNT, Raven's Progressive Matrices). Atypical hand posturing was inversely associated with performance on all neuropsychological measures with the exception of one D-K Number Sequencing task. Presence of autonomic features was not associated with any pattern of neuropsychological performance.

Conclusions: Traditional and atypical neurological exam findings are exhibited in the majority of autistic adults, with atypical speech/language and atypical gaze patterns present in approximately half and repetitive movements in approximately a third of the subjects in this sample. Additional neurological exam findings were identified in the majority of subjects, with approximately a third or more of subjects exhibiting findings of atypical hand posturing, atypical gait, autonomic features or tremor. Exam findings traditionally associated with autism were associated with worse performance on verbal memory, verbal fluency, naming and executive tasks. Of the additional neurological exam findings reported, atypical gait and hand posturing were associated with worse performance on multiple neuropsychological measures. The atypical hand posturing may represent a subtle manifestation of abnormal tone or an evolution of more traditional repetitive movements. The non-traditional exam findings presented here offer additional opportunities to explore and potentially treat manifestations of ASDs into adulthood.

**153.011 11** Adult Outcomes in Typically-Developing Siblings of Individuals with an ASD with Respect to Childhood Parentification. E. C. Fair*, T. S. Tomeny and T. D. Barry, *The University of Southern Mississippi*

Background: Research examining the outcomes of sibling parentification (taking on responsibilities and caregiving duties typically reserved for parents) in typically-developing individuals who have a sibling with ASD remains unclear. Some researchers have suggested that parentification or increased responsibilities in typically-developing siblings could lead to negative outcomes (Barak-Levy et al., 2010) including poor sibling

relationships (Seltzer et al., 2009) or later depressive symptoms and psychological distress (Hooper et al., 2011). However, research also shows that siblings who experienced sibling-focused parentification exhibited fewer negative outcomes than siblings who experienced parent-focused parentification, and siblings who reported higher levels of perceived benefits of parentification experienced lower levels of psychopathology (Hooper et al., 2011).

Objectives: This study sought to examine parentification in typically-developing adult siblings in more detail. It was predicted that sibling-focused parentification and high perceived benefits of parentification would relate to positive outcomes with respect to the adult sibling relationship and psychological functioning, whereas parent-focused parentification would relate to negative outcomes in these areas.

Methods: Fifty-three typically-developing adult siblings [85% female; ages 18-68 ($M$ = 30.58, $SD$ = 13.7)] of individuals with an ASD participated. Siblings completed a demographic form, the Parentification Inventory (PI; Hooper, 2009) to assess childhood history of parentification, the Lifespan Sibling Relationship Scale (LSRS; Riggio, 2000) to assess attitudes toward the sibling relationship, and the Depression Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995) to assess current depressive, anxious, and stress symptoms.

Results: Generally speaking, parent-focused parentification appeared to be unrelated to sibling relationship attitudes. The one exception was a significant positive correlation between parent-focused parentification and adult sibling relationship behavior ($r$ = .34; $p$ = .01). Alternatively, sibling-focused parentification positively related to adult affective ($r$ = .34; $p$ = .01), behavioral ($r$ = .47; $p$ < .001), and cognitive ($r$ = .37; $p$ = .01) relationship aspects, as well as child affective ($r$ = .40; $p$ = .003), behavioral ($r$ = .39; $p$ = .003), and cognitive ($r$ = .48; $p$ < .001) relationship aspects. Furthermore, perceived benefits of parentification were positively related to adult affective ($r$ = .41; $p$ = .002), behavioral ($r$ = .41; $p$ = .002), and cognitive ($r$ = .50; $p$ < .001) relationship aspects and child affective ($r$ = .58; $p$ < .001), behavioral ($r$ = .41; $p$ = .003), and cognitive ($r$ = .58; $p$ < .001) relationship aspects. Also, parent-focused parentification was significantly related to increased levels of anxiety ($r$ = .36; $p$ = .01) and increased levels of stress ($r$ = .38; $p$ = .01). However, sibling-focused parentification was not significantly related to symptoms. Perceived parentification benefits were significantly negatively related to current depressive ($r$ = -.50; $p$ < .001) and stress symptoms ($r$ = -.34; $p$ = .01).

Conclusions: Parent-focused parentification may be related to poorer psychological well-being in adults, whereas sibling-focused parentification and perceiving benefits of parentification relate to better sibling relationships, indicating a possible positive, protective role against later distress. These findings indicate a potential intervention point when working with those with an ASD and their families.

**153.012 12** Empathy Modulates the Reward Value of Mimicry: Implications for Imitation Based Interventions for Autism. J. Neufeld*[1], A. Barry[1], V. Levrini[2] and B. Chakrabarti[1], (1)*University of Reading*, (2)*University of Cambridge*

**Background:** A number of behavioural interventions for children with autism use imitation-based methods to teach social skills (e.g. Early Start Denver Model, Reciprocal Imitation Therapy). However, the mechanism of action for these imitation-based methods is not well established. Social psychological studies have shown that people demonstrate greater liking for those who imitate them, suggesting that imitation/mimicry may alter reward value of social targets (Stel et al., 2008; Stel and Vonk 2010; van Baaren et al., 2003). Functional MRI studies have suggested that the motor-act of mimicking as well as being mimicked can lead to activation of brain regions related to reward processing (Kuehn et al, 2009, 2011; Lee et al. 2006; Likowski et al 2012; Vrticka et al. 2013). These studies lead to the hypothesis that mimicry alters the reward value of a face.

**Objectives:** To directly test the reward value of mimicry, we measured the impact of being mimicked on preferential looking, using gaze duration as a proxy measure of reward consumption (i.e. longer gaze duration is associated with higher reward value). We further tested individual variability in this effect, as a function of trait empathy (as measured by Empathy Quotient, (EQ)).

**Methods:** 37 neurotypical adults (17 males) underwent a conditioning experiment in which they performed facial expressions (happy, sad, or neutral). Crucially, <1s after they started making the expression, they saw a video of a person making the same expression (Mimicking face) or another person making a different expression (AntiMimicking face). In the test phase, pairs of 'Mimicking face' and 'AntiMimicking face' were presented side-by-side on a gaze-tracking monitor. Further, subject's ability to empathise was assessed via the Empathy Quotient (EQ). To ensure that any observed differences were not related to greater response conflict associated with a given face, we conducted a separate experiment (N=19) investigating the effect of spatial congruency on gaze behaviour.

**Results:** Participants showed longer gaze duration for Mimicking faces than AntiMimicking faces after conditioning, (controlling for any baseline difference in looking times for the two faces) (t=2.99, p=.005). No such pattern was detected when comparing spatially congruent vs. incongruent faces in the control paradigm. Further, the magnitude of the difference in gaze duration between Mimicking and AntiMimicking faces, was positively correlated with EQ (r=.319; p=.04).

**Conclusions:** These findings suggest that being mimicked by a face changes its reward value, which is indexed by longer gaze durations. This effect is not driven by different levels of response conflict associated with the different faces, as shown by the results of the control task. Further, this effect is greater in more empathic individuals, suggesting that empathy affects the interaction between mimicry and reward system, i.e. this link seems to be stronger in individuals with higher EQ. These results provide direct evidence for a potential reward-based mechanism through which imitation-based interventions in autism may work, and identify key dimensions of individual variation.

## 154 Animal Models

**154.013 13** A Goldilocks Effect for Ube3a in Regulating Social Behavior Via Altered Gene Expression in Idic15 Autism and Angelman Syndrome. M. P. Anderson*, *Harvard Medical School/Beth Israel Deaconess Medical Center*

**Background**: Increases of *Ube3a* gene dosage cause autism (maternal isodicentric chromosome 15 [idic15], maternal Ube3a triplication), while maternal *Ube3a* loss causes Angelman syndrome. In mature neurons, Ube3a is expressed exclusively from the maternal allele. In neurons, paternal *Ube3a*expression is repressed. Ube3a acts as an E3 ubiquitin ligase but also, independently, as a transcriptional co-activator.

**Objectives**: Whether excess Ube3a in the neuronal synapse, cytoplasm, or nucleus causes autism is unknown. Furthermore, clinically, Idic15-associated autism and Angelman syndrome appear to have diametrically opposite social behavioral features. Can this idea be reinforced through studies of this behavior in mouse models of the disorders?

**Methods**: To clarify, we engineered a nuclear importing peptide signal to the C-terminus of *Ube3a*. We also examined the effects of changes in Ube3a gene dosage on transcription and social behavior.

**Results**: Mice with just a single added copy of nuclear-imported *Ube3a* displayed the full autism-type behavioral deficits in social interaction and communication generated by two copies of non-targeted *Ube3a* that models idic15. In contrast, mice with a deleted maternal *Ube3a* displayed increased social behavior, consistent with the reported increased social laughter, smiling, and interaction of individuals with Angelman syndrome. *Ube3a*dose-dependently altered cortical mRNAs mirroring its effects on social behavior. Direct protein-protein interactions between products of the Ube3a-regulated and all known autism deleted, duplicated, or mutated (missense) genes, identified pivotal Ube3a-regulated genes in an autism protein-interaction network.

**Conclusions**: By comparing idic15 autism and Angelman, we uncover a Goldilocks effect for *Ube3a* in controlling cortical gene expression and social behavior. Furthermore, by targeting Ube3a to the nucleus, we link dysregulated gene expression to autism.

**154.014 14** Pten Haploinsufficient Mice Show Selective Impairments in Autism-Relevant Behavioral Tests. A. E. Clipperton-Allen* and D. T. Page, *The Scripps Research Institute*

Background: *Phosphatase and tensin homolog* (*PTEN*) is one of several genes encoding negative regulators of the PI3K-Akt-mTOR pathway that have been identified as autism

spectrum disorder (ASD) risk factors. Mutations in *PTEN* have been reported in individuals with ASD and macrocephaly. Using a mouse model of *Pten* germline haploinsufficiency (*Pten*$^{+/-}$), we previously found that mutant mice show both deficits in social approach behavior and brain overgrowth.

Objectives: The distribution of *Pten* mRNA in the brain is broad, as is the brain overgrowth in *Pten*$^{+/-}$ mice. However, it is not known if this translates into broad effects on behavior in these mice, or if effects are restricted to specific domains or vulnerable neural systems. Our aim is to fill in this gap in our knowledge.

Methods: We tested male and female *Pten*$^{+/-}$ mice on ASD-relevant behaviors (social behavior: social approach, social novelty, social recognition; repetitive, stereotyped behavior: marble burying), as well as assays related to ASD comorbidities (mood disorders: tail suspension test, forced swim test; anxiety disorders: dark-light emergence, open field test; emotional learning and memory: trace fear conditioning; sleep disorders: circadian rhythm and activity) and relevant control measures (hotplate, rotarod).

Results: *Pten*$^{+/-}$ mice showed decreased social approach and social novelty, and impaired social recognition as assessed by habituation/dishabituation, as well as brain overgrowth. Male *Pten*$^{+/-}$ mice buried more marbles (suggesting an increase in repetitive behavior), showed increased immobility in tail suspension and forced swim tests (indicating increased depression-like behavior), and increased center and light chamber time in the open field and dark-light emergence tests, respectively (indicating decreased anxiety-like behavior). We also found that *Pten*$^{+/-}$ females exhibited abnormalities in circadian rhythm and activity and emotional learning. Our results suggest that *Pten* may function in dopamine (DA) neurons to affect behavior; thus, we tested mice in which *Pten* has been inactivated in DA neurons via the *Cre-loxP* system (DAT-*Pten*-cKO) on social behavior assays. Results from this experiment indicate that DAT-*Pten*-cKO mice may also show impairments in social behavior.

Conclusions: We found that the behavioral phenotypes present in *Pten*$^{+/-}$ mice are selective, despite the broad distribution of *Pten* mRNA and overgrowth in the brain. This suggests that specific neural systems are vulnerable to disruption by *Pten* mutations. One possible system through which this disruption may be affecting behavior is the DA system; our results indicate that conditional inactivation of *Pten* in neurons of this system may lead to social behavioral deficits. Ongoing studies are exploring the involvement of dopaminergic neurons and other cell types in behavioral deficits resulting from mutation of *Pten*.

**154.015 15** Cyfip1 Developmentally Regulates Presynaptic Function. K. Hsiao*[1], H. Harony-Nicolas[2], J. D. Buxbaum[1], D. L. Benson[1] and O. B. Gunal[1], (1)*Icahn School of Medicine at Mount Sinai*, (2)*Seaver Autism Center for Research and Treatment*

Background: Copy number variations in the gene encoding Cyfip1 are associated with several neurodevelopmental disorders and altered levels of Cyfip1 may correlate with increased disease severity. A common feature of several disorders is defective synapse development or function and work from our labs and others indicates that Cyfip1 plays a role in both normal synapse development and plasticity. Cyfip1 has independent actions as a regulator of protein translation and of actin polymerization, but how changes in Cyfip1 levels could contribute toward or exacerbate neurodevelopmental brain disorders is poorly understood.

Objectives: To test the impact of changing Cyfip1 levels on synapse development and function alone and via its interactions with Fmrp.

Methods: In order to test effects of Cyfip1 levels and genetic interaction between Cyfip1 and Fmr1, we crossed heterozygous mice and evaluated presynaptic and postsynaptic function in acute hippocampal slices at different ages from 4 different groups and in neuronal cultures. We applied a combination of FM4-64 imaging, biochemical, immunohistochemical and electrophysiological techniques in mouse tissue, principally focusing on hippocampal area CA1.

Results: In neurons cultured from *Cyfip1*$^{+/-}$ mice, developing synapses showed abnormal presynaptic properties. Assessments of vesicle recycling using FM4-64 uptake and release revealed an increase in recycling pool size and release kinetics than in neurons cultured from wild type littermates. *Cyfip1*$^{+/-}$ knockdown in individual

neurons indicates that this effect is cell autonomous and generated presynaptically with no detectable impact on the generation of postsynaptic densities (labeled with PSD95). The effect on presynaptic function in cultured neurons is reflected in abnormal paired-pulse ratio measurements of presynaptic function and mEPSCs in hippocampal slices from P10 animals—effects that are absent at mature synapses. At mature synapses, the major impact of Cyfip1 levels is reflected in altered plasticity and reflects at least in part that Cyfip1 partners with Fmrp and regulates protein translation. Our previous results show that mice lacking one functional copy of *Cyfip1* exhibit enhanced hippocampal mGluR-LTD in 4-6 week old mice similar to Fmr1 knockout mice. In double mutant mice (*Cyfip1*$^{+/-}$; *Fmr1*$^{-/y}$) mGluR-LTD is enhanced similar to single mutants (a phenotype that is absent in young synapses). However, Fmrp and Cyfip1 levels are not regulated by each other. Double mutant mice also show significantly reduced HFS (high frequency stimulus)-induced LTP and LFS (low FS)-induced GluN-LTD, which suggests an additive or interactive effect of Fmrp and Cyfip1. To confirm that decreased levels of Cyfip1 influence actin polymerization, we compared polymerized and soluble actin fractions isolated from hippocampal lysates in WT and *Cyfip1* heterozygous mice, which showed and increase in the ratio of F- to G-actin in *Cyfip1* heterozygous mice.

Conclusions: These data demonstrate that Cyfip1 reduction has a strong effect on presynaptic function in young neurons, distinct from Fmrp action, but has an interactive effect with Fmrp in the regulation of postsynaptic function in mature synapses. Altered levels of Cyfip1 may affect the mechanisms underlying a developmentally regulated switch from pre to postsynaptic phenotypes and contribute to increased disease severity.

**154.016 16** Developmental Trajectory and Parental Behaviour Contribution to the Advanced Paternal Age Effects on Autism-Related Phenotypes in Mice. M. Janecka*[1], A. Manduca[2], R. Smith[1], L. Schalkwyk[1], J. Mill[1], V. Trezza[2], A. Reichenberg[1] and C. Fernandes[1], (1)*King's College London*, (2)*Roma Tre University*

Background:

Advanced paternal age (APA) has been reliably linked to a host of adverse outcomes in offspring, ranging from congenital spontaneous conditions to complex disorders like schizophrenia and autism. Previous studies reported deficits in several behavioural domains in the mouse models of APA, but not their developmental trajectory; also, they failed to show unequivocally that these effects arise de novo in offspring, rather than are parentally-inherited.

Objectives:

Our study used inbred C57BL/6J mice to investigate the effects of APA on offspring, both during early development and in adulthood, focusing on the behavioural domains in which autistic individuals show impairment. Parental behaviour was also assessed in order to eliminate possible confounding factors.

Methods:

Three groups of offspring of (i) young (8 weeks old fathers), (ii) old (40 week old fathers) and (iii) very old fathers (48 week old fathers) were tested through a battery of behavioural tasks. The tests assessed both early development (emergence of critical reflexes, motor and physical landmarks, and social development), and behaviour in adulthood. The latter battery included following tests: homecage (locomotor activity), open field (anxiety), holeboard (exploration), 3 chamber social approach (social preference), social interaction, olfactory habituation/dishabituation (olfaction and olfactory memory), marble burying test (repetitive behaviour), rotarod (motor learning) and Morris water maze (spatial learning and memory). Majority of the tests run on adult offspring also were run on fathers, in order to eliminate paternal effects that were not related to the father's age at conception. Also, a separate battery was designed for mothers, to assess the effects of potentially confounding maternal effects on pup development.

Results:

We have observed differences in motor and social domains in the offspring of old and very old fathers, both early in development and in adulthood. No corresponding group differences in paternal behaviour or dam-pup interactions were recorded.

Conclusions:

Offspring of old and very old fathers displayed differences in social and motor domains, which are often affected in individuals with autism. These were visible already at postnatal days 10-21, and persisted till adulthood, underscoring the importance of looking at developmental trajectories in mouse models. None of these effects could be reliably explained by parental behavioural profiles, suggesting that APA effects arise de novo in the offspring generation. Further investigation will try to elucidate whether these effects can persist through generations (three generations will be tested in total) and if a perinatal dietary intervention (folic acid enrichment) can reverse them.

**154.017 17** Behavioral Consequences of Disrupted MET Signaling. B. Thompson*[1], W. Rodriguez[2] and P. Levitt[1], (1)*University of Southern California*, (2)*Childrens Hospital of Los Angeles*

Background: Utilizing genetically modified mouse lines to dissect the role of specific genes in the neurobiological underpinnings of neurodevelopmental disorders is an important approach. Our laboratory discovered that the gene encoding the receptor tyrosine kinase, *MET*, contributes to autism risk. Subsequent studies have shown a role for *MET* in functional and structural cortical connectivity in typically developing individuals and those with autism spectrum disorder. Furthermore, our studies have illuminated a role for *Met* in dendritic and spine architecture and excitatory drive in the cortex of mouse models of altered Met signaling. To further understand the contribution of Met to brain development and its impact on behavior, we generated two conditional mouse lines in which *Met* is deleted from select populations of cerebral cortex neurons. These mice were then tested to determine the developmental and long-term behavioral consequences of disrupting Met signaling.

Objectives: The objective of these studies was to test our hypothesis that disruption of Met signaling during development has functional consequences on the maturation of cortical circuits and behaviors that are altered in autism. These studies define autism relevant specific social, emotional and cognitive behaviors caused by developmental disruption of Met cortical signaling.

Methods: We generated two conditional mouse lines in which *Met* is deleted from select populations: 1) $Met^{fx/fx}/Emx1^{cre}$ (deleted from all cells arising from the dorsal pallium) and 2) $Met^{fx/fx}/Nestin^{cre}$ (deleted from all neural cells). A battery of behavioral tests was performed to assess cognitive, emotional, and social impairments that are observed in multiple neurodevelopmental disorders, including ASD, and that, are in part sub-served by circuits that express Met. Multiple cohorts of n=6 mice per genotype were tested in early adulthood on rotarod, activity chamber, elevated plus maze, spontaneous alternation in the t-maze, olfactory dishabituation, social novelty preference, marble burying, and contextual fear conditioning.

Results: Across multiple cohorts of animals we found that the null $Met^{fx/+}/Emx1^{cre}$ mice display significant hypoactivity in the activity chamber and in the t-maze despite normal performance on the rotarod. Additionally, these animals show a deficit in spontaneous alternation. The null $Met^{fx/+}/Emx1^{cre}$ mice show normal anxiety, olfactory dishabituation, social novelty preference, contextual fear conditioning, and marble burying. The null $Met^{fx/fx}/Nestin^{cre}$ mice display deficits in contextual fear conditioning, and a weak deficit in sociability in the social novelty preference task. The null $Met^{fx/fx}/Nestin^{cre}$ mice show normal performance on rotarod and activity chamber, anxiety, spontaneous alternation, olfactory dishabituation, and marble burying.

Conclusions: These data suggest a complex contribution of Met in the development of social, emotional, and cognitive behavior. The impact of disrupting developmental Met expression is dependent upon the circuit-specific deletion pattern. The null $Met^{fx/fx}/Nestin^{cre}$ mice (*Met* deleted from every cortical cell) show behavioral phenotypes consistent with autism. In contrast, the null $Met^{fx/+}/Emx1^{cre}$ mice (*Met* deleted from all cells arising from the dorsal pallium) show a different behavioral phenotype, with decreased exploratory behavior and memory. Future studies will determine the impact of environmental interactions with the deletion of Met from the $Met^{fx/fx}/Nestin^{cre}$ mice on further social, emotional, and cognitive behaviors.

**154.018 18** Differences in Neuronal Activation and Gene Expression in the Fragile X Mouse. T. D. Rogers*, C. G. Forsberg and J. Veenstra-Vander Weele, *Vanderbilt University*

Background: Abnormal social behavior is a core symptom of autism spectrum disorders (ASD) and

fragile X syndrome (FXS). Interestingly, previous studies have demonstrated an association of amygdala activation with both social approach and social avoidance behavior. Further, both functional and structural neuroimaging studies have implicated the amygdala and PFC in ASD. It is currently unclear whether molecular changes occurring in the amygdala and PFC could mediate altered social behavior observed in ASD and FXS. We used the *Fmr1* knockout (KO) mouse, which displays altered social behavior, to further investigate this relationship.

Objectives: 1) Determine the impact of a loss of *Fmr1* expression on neuronal activation patterns in amygdala and PFC following exposure to a social stimulus. 2) Identify gene expression changes in the amygdala and PFC of *Fmr1* KO mice in response to social challenge.

Methods: *Fmr1* KO mice and littermate controls were exposed to a behavioral challenge that parallels the 3-chamber sociability test but separates the exposures so that a subject mouse encounters either a novel mouse or a novel object. We used immediate early gene activation (cFos) immunohistochemistry and compared neuronal activation patterns in different brain regions across conditions and genotypes. RNA sequencing of the lateral amygdala, medial amygdala, and PFC in each condition and genotype is underway.

Results: Presentation of a novel mouse, as compared to the presentation of a novel item, elicited increased levels of activation in the lateral and medial amygdala and decreased levels of activation in the PFC in wildtype animals ($p < .05$). *Fmr1* KO mice displayed increased neuronal activation in lateral and medial amygdala across both behavioral conditions as compared to littermate controls ($p < .01$). Also, *Fmr1* KO mice displayed decreased activation of PFC across both behavioral conditions as compared to littermate controls ($p < .05$). RNA sequencing results will also be presented.

Conclusions: The current findings indicate that both the amygdala and the PFC display differences in neuronal activation patterns in response to social stimuli in comparison to non-social stimuli. *Fmr1* KO mice display exaggerated responses in both brain areas that could underlie altered social behaviors. Differences in gene expression in these two brain areas in response to social challenge may suggest a mechanism for the changes in neuronal activation patterns and behavioral responses.

**154.020 20** Distribution of Oxytocin Receptors and Vasopressin 1a Receptors in the Titi Monkey, an Emerging Animal Model for the Study of Social Attachment. S. M. Freeman*[1], L. J. Young[2] and K. L. Bales[1], (1)*University of California, Davis*, (2)*Emory University*

Background: Oxytocin (OT) and vasopressin (AVP) are structurally related neuropeptides that act in the brain to modulate the expression of species-specific social behaviors. Research in this field has plowed ahead to investigate the effects of OT in humans, including individuals with autism spectrum disorder (ASD), despite a lack of understanding of the fundamental neurophysiology of these systems in humans and nonhuman primates (NHP) alike. Studying the brains of NHP provides an opportunity to elucidate the neural mechanisms by which OT and AVP modulate social cognition. The coppery titi monkey is a socially monogamous New World primate that has been used to investigate the behavioral neuroendocrinology of social attachment. By establishing the neurochemical basis of pair bonding in this monogamous species, we can better understand how the brain coordinates complex social behaviors more broadly, such as selective attachment, cooperation, and social memory. This research provides valuable insight into the mechanisms underlying social behavior in humans, which can then lead to the development of better treatments for individuals diagnosed with ASD.

Objectives: To identify the distribution of the oxytocin receptor (OXTR) and vasopressin 1a receptor (AVPR1a) in order to provide a neuroanatomical foundation for the study of these neuropeptides in mediating social behavior in primates.

Methods: We used a pharmacologically optimized, competitive-binding receptor autoradiography protocol to identify the distribution of OXTR and AVPR1a in hemispheres of titi monkey brain (n=5). In this procedure, either the AVPR1a radioligand ($^{125}$I-LVA) or the OXTR radioligand ($^{125}$I-OVTA) was incubated on tissue in one of three conditions: 50 pM radioligand alone, or in the presence of either 10 nM of a selective human AVPR1a ligand

(SR49059) or 20 nM of a selective human OTR ligand (ALS-II-69).

Results: The AVPR1a distribution is widespread throughout the brain, but the OTR distribution is much more limited, with the most abundant binding in the hippocampus, dentate gyrus, presubiculum, nucleus basalis of Meynert, and several hindbrain regions. AVPR1a binding exists throughout the cortex (especially cingulate and occipital cortex), as well as in the caudate, putamen, hippocampus, globus pallidus, lateral geniculate nucleus, periaqueductal grey, substantia nigra, olivary nucleus, and cerebellum. Furthermore, we show that ALS-II-69 reduces OXTR radioligand binding by 40-50% without affecting AVPR1a binding, and that SR49049 is capable of reducing AVPR1a radioligand binding by 75% or more, without significantly affecting binding to OXTR.

Conclusions: Both receptors are found in brain regions that modulate visual attention and control orienting responses to visual stimuli. This has important implications for 1) the development of therapies to improve social visual attention and 2) our understanding of neural mechanisms underlying social gaze. Furthermore, both ALS-II-69 and SR49049 emerge as candidates for the pharmacological manipulation of OXTR and AVPR1a in future behavioral experiments in titi monkeys and other primates. These results can ultimately facilitate the development of pharmacological strategies to target the OT and AVP systems for the improvement of social function in individuals with ASD.

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**154.021 21** Hippocampal Dysregulation of Neurofibromin-Dependent Pathways Is Associated with Impaired Spatial Learning in Engrailed 2 Knockout Mice. G. Provenzano*[1], L. Pangrazzi[1], A. Poli[2], P. Sgadò[1], S. Genovesi[1], G. Zunino[1], N. Berardi[2], S. Casarosa[1] and Y. Bozzi[1], (1)*Centre for Integrative Biology (CIBIO), University of Trento, Italy*, (2)*C.N.R. Neuroscience Institute, Pisa, Italy*

**Background:** Genome-wide association studies indicated the homeobox-containing transcription factor Engrailed-2 (En2) as a candidate gene for autism spectrum disorders (ASD). Accordingly, En2 knockout (En2-/-) mice show anatomical and behavioural "ASD-like" features, including decreased sociability and learning deficits. The molecular pathways underlying these deficits in En2-/- mice are not known. Deficits in signaling pathways involving neurofibromin and extracellular-regulated kinase (ERK) have been associated to impaired learning.

**Objectives:** Here we investigated the neurofibromin-ERK cascade in the hippocampus of wild-type (WT) and En2-/- mice before and after spatial learning testing.

**Methods:** Twenty-two mice (11 per genotype) were used for the MWM. Animals were killed at the end of MWM and brains dissected: for RT-PCR and immunoblotting, 4 hippocampi per genotype were dissected and frozen in dry ice; for immunohistochemistry, 4 brains per genotype were fixed by 4% paraformaldehyde perfusion; for in situ hybridization, 3 brains per genotype were frozen on dry ice. An additional group of age-matched, naïve mice (8 per genotype) were not subjected to MWM and used a controls.

**Results:** When compared to WT littermates, *En2-/-* mice showed impaired performance in the Morris water maze (MWM), which was accompanied by lower expression of the activity-dependent gene *Arc*. Quantitative RT-PCR, immunoblotting and immunohistochemistry experiments showed a marked downregulation of neurofibromin expression in the dentate gyrus of both naïve and MWM-treated *En2-/-* mice. ERK phosphorylation, known to be induced in the presence of neurofibromin deficiency, was increased in the dentate gyrus of *En2-/-* mice after MWM.

**Conclusions:** Dysregulation of the neurofibromin/ERK pathway in the hippocampus may contribute to spatial learning deficits in the En2 mouse model of ASD.

**154.022 22** R-Baclofen, a Gabab Agonist, Reduced Stereotyped and Repetitive Behavior in the BTBR and C58 Mouse Models of Autism. J. L. Silverman*, M. C. Pride, J. E. Hayes and J. N. Crawley, *University of California Davis School of Medicine*

**Background:** A fundamental hypothesis in the search for causes of autism spectrum disorder (ASD) focuses on dysregulation of the excitatory/inhibitory balance in the brain. Reducing excitatory glutamatergic transmission,

and/or elevating GABAergic inhibition, could normalize the excitatory/inhibitory balance. This theory is supported by electrophysiological studies in mouse models with mutations in risk genes for autism, in which excessive glutamatergic excitation or impairments in synaptic plasticity are common. Furthermore, clinical trials of positive and negative modulators of glutamatergic and GABAergic receptors are being pursued.

**Objectives:** The specific objective of this proposal is to test the hypothesis that enhanced inhibitory transmission, via the $GABA_B$ agonist $R^+$-baclofen, will reduce high levels of repetitive behavior in two mouse models of non-syndromic autism. BTBR displays multiple behavioral phenotypes with face validity to both of the diagnostic symptoms of autism, including well-replicated low sociability, low levels of vocalizations in social settings, and high levels of repetitive self-grooming. $R^+$-baclofen was similarly tested in C58/J mice (C58), which display high levels of stereotyped jumping and repetitive grooming. The control strain, C57BL/6J (B6), displays high sociability and no detectable stereotyped or repetitive behaviors.

**Methods:** BTBR, C58 and B6 were given an intraperitoneal injection of $R^+$-baclofen (1.0 mg/kg, or 3.0 mg/kg) or saline, 30 or 60 minutes before behavioral testing. BTBR, C58 and B6 were tested in three behavioral tasks: 1) marble burying in an empty mouse cage (Thomas et al., 2012), 2) self-grooming in a clean standard mouse cage for a 10 minute test session (Silverman et al., 2012) and 3) open field locomotor activity, as a control measure to detect confounding drug-induced behavioral sedation.

**Results:** $R^+$-baclofen reduced repetitive self-grooming and marble burying in two cohorts of BTBR mice. $R^+$-baclofen also reduced stereotyped jumping in C58 mice. Effective doses of $R^+$-baclofen on repetitive or stereotyped behavior in BTBR or C58 mice did not produce signs of sedation, as measured in the open field locomotor exploration test, 1 hour post drug administration.

**Conclusions:** Two mouse models of non-syndromic ASD provide corroborative preclinical evidence that a $GABA_B$ agonist may be effective for decreasing stereotyped and repetitive and behaviors in autism spectrum disorder.

**154.023 23** The Role of Transglutaminase 2 in GABAA Receptor Regulation in Autism. A. M. Crider*, C. Pandya and A. Pillai, *GRU*

Background: Autism is a neurodevelopmental disorder affecting 1 in 88 children in America and is approximately 5 times more common in boys than girls. Deficits in GABAergic neurotransmission have been implicated in the pathophysiology of autism. The strength of synaptic inhibition can be determined by the number of γ-amino butyric acid type A receptors ($GABA_A$Rs) found at synaptic sites. The role of $GABA_A$Rs in autism is substantiated by studies showing decreased $GABA_A$R subunit $\alpha_1$ ($GABA_A$R $\alpha_1$) protein levels in the prefrontal cortex (PFC) of subjects with autism. However, the molecular mechanisms that regulate $GABA_A$R $\alpha_1$ trafficking in autism remain unclear. Our goal is to determine the role of transglutaminase 2 (TG2) in the regulation of $GABA_A$R $\alpha_1$ signaling. TG2 is a calcium-dependent enzyme that plays an important role in posttranslational modification of proteins. Recent studies have indicated that calnexin, an endoplasmic reticulum chaperone involved in $GABA_A$R α1 regulation is a TG2 binding partner.

Objectives: Our long term goal is to understand the regulatory mechanism of GABAAR signaling in autism as a prerequisite to the development of therapeutic protocols that can be used to attenuate the disease process. The objective of this proposal is to determine the role of transglutaminase 2 (TG2) in the regulation of $GABA_A$R $\alpha_1$ signaling. The specific hypothesis behind the study is that increased TG2-dependent degradation of $GABA_A$R $\alpha_1$ inhibits GABAergic neurotransmission with autism-like phenotype in mice.

Methods: Human postmortem prefrontal cortex samples from ASD/Autism and control subjects were obtained from NICHD. Animal experiments were performed in C57BL/6 mice overexpressing Transglutaminase 2 in neurons and wild-type. In vitro studies were performed in isolated cortical neurons as well as HEK293 cell line. Protein levels were measured by western blotting, mRNA levels were measured by RT-PCR, TG2 activity was measured by transglutaminase activity assay kit from Sigma. Behavioral measures included open field, tail suspension, forced swim test, social interaction test, and marble bury test.

Results: We found that mice with neuronal TG2 overexpression ($TG2^{+/+}$) show autism-like phenotype with reduced $GABA_AR\ \alpha_1$ protein levels in the frontal cortex. Increases in mRNA, protein, and activity of TG2 were found in PFC of subjects with autism. Moreover, we observed a significant reduction in $GABA_AR\ \alpha_1$ protein levels, but not mRNA in PFC of subjects with autism suggesting $GABA_AR\ \alpha_1$ degradation at the posttranscriptional level. Interestingly, we found significant increases in calnexin in PFC of subjects with autism. Additional studies indicated a role of calnexin in $GABA_AR$ regulation in our model.

Conclusions: Our data suggests that calnexin functions downstream of TG2 and is involved in $GABA_AR\ \alpha_1$ regulation in autism. We further demonstrate that TG2-dependent degradation of $GABA_AR$ induces autism-like phenotype in mice and that calnexin mediates TG2-induced $GABA_AR$ endocytosis. Given the important role of $GABA_AR$ in neuroplasticity, these findings on the regulatory mechanisms of $GABA_AR$ may provide avenues to develop newer therapeutics for autism and related neurodevelopmental disorders.

**154.024 24** Toll-like Receptor-Selective Placental Vulnerability in an Autism Mouse Model. H. M. Moon*, V. Saravanapandian, G. Subramanyam, T. Cisneros, M. Ozen, P. Carpentier, M. Rivera and T. Palmer, *Stanford University*

Background: Autism spectrum disorder (ASD) is a neuro-developmental disease with deficits in social cognition in the child. There is increasing evidence for an innate immune dysfunction in ASD and epidemiological studies suggest that environmental risks such as infections or other gestational immune events correlate with increased ASD risk. Innate immune responses are evoked by toll-like pattern recognition receptor (TLR) signaling pathways. The TLR receptor family members are selective for specific classes of pathogens and it is not known whether different TLRs trigger distinct immune mechanisms in the developing fetus with unique neuropathological outcomes.

Objectives: Our objective is to determine if TLR selective responses have distinct effects on fetal-maternal interaction during early pregnancy in the mouse. Our recent studies suggest that TLR4 activation leads to cortical patterning defects in adult offspring born from maternal immune activation (MIA)-challenged pregnant mothers (Carpentier et al. 2013). We hypothesized that placental pathogenesis evoked by TLR4 activation may selectively alter fetal brain development through hypoxia-related mechanisms while the activation of other TLRs may not.

Methods: Pregnant mice were challenged with different TLR agonists at embryonic day 12.5 (E12.5) during mid-gestation and we analyzed the pregnancy outcomes and fetal brain phenotypes. After systemic prenatal insults such as bacterial (TLR4) and viral (TLR3) infection-mediated MIA responses, we examined placental pathology and neocortical alterations in the developing fetuses, including neural progenitor cell proliferation, cell cycle alterations, and stem cell niche signaling molecules in TLR-challenged animals compared with saline-injected control animals.

Results: Activation of different TLRs led to distinct alterations in placental pathology and fetal growth in early development. The cryoarchitecture of the developing cerebral cortex was severely affected by several specific TLR challenges with unique immune cytokine profiles. Proliferation and divisions of neural progenitor cells were impaired by prenatal insults with specific TLR activation. Acute effects on neurodevelopmental processes were pronounced in TLR4-challenged animals suggesting significantly higher risk of neuropathology from bacterial infections during pregnancy than for other classes of immunogen.

Conclusions: Our data suggests that alterations in early cortical development may be distinct for each class of maternal immune response. Therefore, despite the behavioral similarities of adult animals, there are significant differences in the severity and the type of defects in cortical patterns induced by each TLR-dependent pathway. The data indicate that various TLR pathways may contribute unique immune-related alterations in the fetal-maternal interface and in early brain development.

## 155 Brain Structure

**155.025 25** Atypical Cerebral Lateralization of Language and Motor-Related Regions in High-Functioning Male Adults with Autism. D. L. Floris*[1], M. C. Lai[2], J. Suckling[2], M. V. Lombardo[3], C. Ecker[4], B. Chakrabarti[5], S. J. Wheelwright[6], B. Auyeung[2], C. Allison[2], A. N. Ruigrok[2], E. Bullmore[2], M. AIMS Consortium[7], D. G. Murphy[4] and S. Baron-Cohen[2], (1)*Autism Research Centre*, (2)*University of Cambridge*, (3)*University of Cyprus*, (4)*Institute of Psychiatry, King's College London*, (5)*University of Reading*, (6)*Autism Research Centre,*

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Background:

One potential neuroanatomical marker of autism spectrum conditions (ASC) is atypical cerebral lateralization. The "left hemisphere dysfunction theory" is based on the notion that individuals with ASC exhibit deficits in functions ascribed to the left hemisphere such as language, communication and motor skills whilst appearing relatively unaffected in cognitive functions mainly supported by the right-hemisphere.

Objectives:

To investigate in individuals with autism (1) whether atypical structural cerebral lateralization is present in regions integral to language and motor processing and (2) whether atypical lateralization is related to autistic characteristics and language and motor functioning.

Methods:

Participants comprised 67 adult males with autism (26 with high-functioning autism [HFA]; 41 with Asperger Syndrome [AS]) and 69 typically developing (TD) males, all aged 18-43 years and the two groups were not significantly different in age and IQ. All participants were right-handed based on the Edinburgh Handedness Inventory. Simulated T1-weighted IR images generated from DESPOT1 MRI scans (at 3T) were preprocessed in SPM8 using the VBM8 toolbox. Region-of-interest analyses were conducted by deriving the mean volume of selected motor (Precentral Gyrus [PG], Supplementary Motor Area [SMA]) and posterior language regions (Superior Temporal Gyrus [STG], Planum Temporale [PT], Angular Gyrus [AG], Supramargninal Gyrus [SG]) using the Harvard-Oxford atlas (Kennedy et al., 1998). Laterality indices of grey matter volumes were defined as: [(right – left) / (right + left)] × 100. Autistic characteristics were assessed using subdomain algorithm scores of the ADI-R and ADOS-G. Language performance was assessed using the Non-Word-Repetition task (Gathercole et al., 1994) and motor performance by the Purdue PegBoard Test (Tiffin et al.1948).

Results:

Among language regions, both the PT ($p=0.012$) and the AG ($p=0.013$) showed stronger rightward lateralization in males with ASC compared to TD males. Rightward asymmetry of the PT was associated with poorer performance on the Non-Word-Repetition Task in males with ASC (Pearson's $r=-0.429$; $p<0.001$).

Among the motor regions, the PG showed stronger rightward lateralization in males with ASC compared to TD males ($p=0.009$). This was not associated with performance on the PegBoard Task, but with higher scores on current autistic communicative, social interaction and imagination difficulties (ADOS-A, $r=0.427$; $p=0.037$; ADOS-B, $r=0.411$, $p=0.046$; ADOS-C, $r=0.430$, $p=0.036$) but only in individuals with HFA and not those with AS. For both PT and PG asymmetries, males with AS were intermediate between those with HFA and TD males.

Conclusions:

Atypical cerebral rightward lateralization is present in male adults with ASC in regions associated with language and motor functions. Specifically, atypical lateralizationin the motor cortex is associated with social-communicative deficits in autism, corresponding to theories suggesting that early motor deficits might underlie the core cognitive symptoms in autism (Mostofsky et al., 2000). Reversal of typical asymmetry in the PT in autism has been consistently reported in previous literature, and here we additionally found a gradation between individuals with and without language delay. This stepwise pattern between diagnostic subgroups also applies to a non-linguistic primary motor region, suggesting the possibility of common underlying neurodevelopmental mechanisms contributing to motor, social and language deficits in autism.

**155.026 26** Anatomical MRI Abnormalities in Autism?. S. Haar[1], S. Berman[1], M. Behrmann[2] and I. Dinstein*[1], (1)*Ben Gurion University*, (2)*Carnegie Mellon University*

Background: Considerable controversy exists regarding the presence and significance of anatomical abnormalities in autism spectrum disorders (ASD), especially in individuals older than 6 years of age. The release of the Autism Brain Imaging Data Exchange (1000+ participants, ages 6-65), offers an unprecedented opportunity to perform large-scale comparisons of

anatomical MRI scans across groups and resolve outstanding questions.

Objectives: To identify anatomical abnormalities evident in MRI scans of individuals with ASD aged 6-35 years in comparison with IQ and gender matched individuals, and to assess their potential clinical significance.

Methods: We built an automated analysis pipeline that co-registered all MRI scans to a single anatomical template and parcellated each subject's brain into over 180 anatomical ROIs using a probablistic atlas. This was performed using Freesurfer image analysis suite and custom written software. Importantly, scans of all subjects were handled in an identical, automated manner so as to avoid potential biases inherent in manually performed analyses.

Results: Comprehensive univariate analyses using anatomical measures from over180 brain areas, revealed only a few significant differences between ASD and control brains, and these were mostly limited to ASD individuals with severe symptoms. Significant between-group differences were on the order of 2-4%, while between-subject differences within each group reached 80-100%. Small differences across groups were, therefore, greatly overshadowed by considerable within-group variability. In agreement with the univariate analyses, several multivariate classification analyses yielded marginal decoding accuracies of ASD and control individuals.

Conclusions: These sobering findings challenge previous reports of anatomical abnormalities in ASD individuals older than 6 years of age, and suggest that anatomical measures derived from MRI scans of these individuals are likely to be of low clinical and scientific significance for ASD research.

**155.027 27** Frontal and Parietal Lobes' Structure Is Associated with Impairments in Motor and Social Skills in Children with Autism Spectrum Disorder. R. Mahajan*[1], B. Dirlikov[1], D. Crocetti[1] and S. H. Mostofsky[2], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins School of Medicine*

**Background:** Electrophysiological and functional imaging studies suggest that frontal and parietal regions may be critical for guiding learning and ongoing behavioral control in children (Gazzaley et al., 2005; Schumacher et al., 2007). Furthermore, the ability to use sensory information to form internal representations of behavior is critical to guiding skilled movements and complex behaviors. Frontal-parietal networks (FPNs), therefore, appear to be important for 1) transposing sensory representations into motor commands, 2) selecting goal oriented movements, and 3) executing movement. FPNs are thereby central in the control of a person's interaction with his/her environment including the planning and organization of sequences of movements necessary to engage in complex social and communicative behavior. Children with autism spectrum disorder (ASD) may have deficits in these abilities. Several studies have implicated frontal and parietal lobe dysfunction in children with ASD (Muller et al., 2001; Haswell et al., 2009) prompting researchers to emphasize the potential contribution of FPNs to the pathophysiology of autism (Just et al., 2007).

**Objectives:** To examine the structure of frontal and parietal regions relevant for formation of internal models of action and their associations with measures of motor function and symptom severity in children with ASD and typically-developing (TD) children.

**Methods:** High resolution T1-weighted MPRAGE images (Slice thickness=1.0 mm) images were acquired in 50 children (42 M) with ASD and 50 (42 M) age, gender, SES, and PRI (WISC-IV) matched TD children, aged 8-12 years. Cortical measurements (thickness, surface area, volume) were examined in Freesurfer using motor, premotor, and parietal ROIs derived from the Desikan (Desikan et al., 2006) and Ranta (Ranta et al., 2009) atlases. MANOVA and MANCOVA were used to examine group effects while covarying for total brain volume (TBV). Pearson's correlations were used to examine motor relevant ROI associations with measures of motor function, assessed using the Physical and Neurological Examination for Soft Signs (PANESS) and the Florida Apraxia Battery, modified for children (Mostofsky, 2006), and autism symptom severity assessed using the ADOS-G and the ADI-R.

**Results:** Children with ASD showed significant bilateral increases in both cortical grey matter volumes (GMV) and cortical surface area (SA) in the inferior parietal cortex, post-central gyrus, and precentral gyrus before and after covarying for TBV. Pearson correlations revealed significant relationships between bilateral primary motor

cortex SA and total PANESS scores, with higher (worse) PANESS score associated with increased SA (r=0.25, p = 0.019). Additionally, bilateral inferior parietal cortex GMV (r=0.268, p=0.062) and bilateral postcentral gyrus GMV (r=0.305, p=0.033) were correlated with higher total ADOS scores.

**Conclusions:** Consistent with previous literature, children with ASD showed increased brain volumes and SA in the frontal and parietal cortices. Furthermore, these increases in regions pertinent to internal action model formation were associated with impaired motor skill learning and control, as well as increased ASD symptom severity. These results support the growing literature on motor dysfunction in ASD and suggest that for children with ASD, dysfunction within FPNs may contribute to impaired development of a range of skilled behavior, including motor and social skills.

**155.028 28** Regional Brain Volume Differences Between Males with and without Autism Are Highly Age-Dependent. H. C. Ni*[1], H. Y. Lin[1], M. C. Lai[2], W. Y. I. Tseng[3] and S. S. F. Gau[4], (1)*National Taiwan University Hospital*, (2)*University of Cambridge*, (3)*National Taiwan University College of Medicine*, (4)*Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine*

Background:

Meta-analyses suggest that the atypical neurobiology of autism may vary substantially with age. This also implies that individuals with and without autism may have different trajectories of brain growth.

Objectives:

To test (1) if brain volumetric differences between individuals with and without autism vary across chronological ages of 7-30 years old, and (2) if the volume of age-dependent atypical brain regions in autism is associated with current social deficits.

Methods:

Voxel-based morphometry (using DARTEL) was applied on structural MRI (3T) images of 104 males with autism (mean=14.6 years, standard deviation, SD=4.4) and 90 typically developing (TD) males (mean=15.0, SD=5.9). A general linear model was used to test if there are significant diagnosis-by-age interaction effects in gray matter (GM) and white matter (WM) volume. If confirmed, main effects of diagnosis among different age-bands would be contrasted in three age-stratified subsamples (TD, autism): children [7-12 years old,, n=44, 37], adolescents [13-17 years old; n=17, 44], adults [18-30 years old; n=29, 23], with age (linear term) covaried in the models. Statistical outcomes were corrected at the cluster-level with topological FDR q<0.05 (corrected for non-stationarity) and cluster-forming voxel-level p<0.001. The Taiwanese Social Responsiveness Scale (SRS) was used to quantify current autistic-like social deficits.

Results:

For absolute total volumes, no significant diagnosis-by-age interaction was detected in GM (p=0.258) or WM (p=0.179). Across ages, males with and without autism did not significantly differ in total GM (p=0.069) or WM (p=0.096) volumes. For both groups, total GM volume decreased (Spearman's Rs=-0.298, p=0.002 in autism, Rs=-0.557, p<0.001 in TD) and WM volume increased (Rs=0.219, p=0.03 in autism, Rs=0.274, p=0.009 in TD) with age. For relative (i.e., corrected for individual total) local GM volume, first in a simple model without considering age and diagnosis-by-age interaction effects, there were only trend-level effects of diagnosis (autism>TD) at bilateral frontal pole and medial prefrontal cortex (mPFC); no significant effects were found in WM. However, in a second model testing for main effects of diagnosis, age, and diagnosis-by-age interaction, significant interaction was identified at again bilateral mPFC, as well as cuneus (mPFC: q<0.001, 6546 voxels, peak-voxel T=5.2; cuneus: q=0.036, 1627 voxels, peak-voxel T=5.0). Here, between 7-30 years old, relative GM volume decreased with age in TD males, but increased with age in males with autism. Age-stratified analyses showed that compared to TD groups, children with autism were smaller in cuneus GM, adolescents with autism were larger in WM at the premotor portion of the corticospinal tract, and adults with autism were larger in mPFC GM. In all individuals with autism, larger relative GM volumes in mPFC and cuneus were both associated with increased 'social awareness' difficulty (derived from an independent factor analysis on the Taiwanese SRS) (mPFC, Rs=0.298, p=0.002; cuneus, Rs=0.241, p=0.015). Other SRS subscores did not show significant correlations.

Conclusions:

Local brain volume differences between males with and without autism vary substantially with age between 7-30 years of age. Males with and without autism may have different brain growth trajectories beyond childhood, which needs to be investigated by future longitudinal studies.

**155.029 29** Cortical Thinning Is Related to Restricted Repetitive Behaviour in Autism Spectrum Disorders. J. E. Fitzgerald*, L. Gallagher, J. McGrath and S. Delmonte, *Trinity College Dublin*

Background: Autism spectrum disorders (ASD) are neurodevelopmental disorders characterised by deficits in two subdomains, social communication and restricted repetitive behaviour as per DSM-V guidelines. Research has suggested that cortical development follows an aberrant trajectory in ASD. Research has shown that brain volume and cortical thickness abnormalities exist in ASD and it has been suggested that these abnormalities may contribute to the traits of ASD.

Objectives: Our research aims to investigate if there is a relationship between measures of cortical integrity (grey and white matter volume, grey and white cerebellar volume, cortical thickness(CT)) and measures of behavioural deficits (social communication deficits (SCD) and fixated interests and repetitive behaviour (FIRB)) in a well-defined ASD sample.

Methods: Freesurfer image analysis software was used was used to generate a cortical surface model to measure brain volume and CT. T-tests and ANOVA were performed to evaluate between group differences on brain volume and CT. Correlation analyses were performed to examine the relationship between SCD, FIRB (Georgiades et al., 2012) and the cortical measures.

Results: The groups did not differ in age ($t(102)=-2.46$, $p=0.806$) or IQ ($t(102)=-1.792$, $p=0.076$). No significant difference was found between groups in terms of cerebral and cerebellar grey and white matter volume, $p>0.05$. A significant difference in CT was observed between groups ($t(102)=-9.8383$, $p<0.001$) and was observed across all lobes, $p<0.001$. In the ASD group, RRB was significantly correlated with the right frontal lobe CT ($r=-0.375$, $p=0.035$) right parietal lobe CT ($r=-0.443$, $p=0.005$) and the left cingulate lobe CT ($r=-0.391$, $p=0.025$) corrected for multiple comparisons. SCD was also inversely correlated with the cingulate lobe CT ($r=-0.318$, $p=0.023$) and positively correlated with right cerebellar white matter volume ($r=0.296$, $p=0.035$) but neither survived correction for multiple comparison.

Results revealed that the ASD group demonstrated reduced cortical thickness in the frontal, parietal, temporal, occipital and cingulate lobes in comparison to the control group. These findings replicate the majority of research demonstrating cortical thinning in ASD. Correlation analyses revealed that restricted repetitive behaviour was inversely related to cortical thickness in the right frontal and parietal lobes as well as the left cingulate lobe, in regions considered necessary for cognitive control and executive functioning.

Conclusions: This study demonstrates that behavioural deficits may be underpinned by structural abnormalities in ASD.

**155.030 30** Neurochemical Concentration, White Matter Integrity, and Brain Functioning in Autism Spectrum Disorder. L. Libero*, T. DeRamus and R. K. Kana, *University of Alabama at Birmingham*

Background: Widespread functional and anatomical alterations have been the main features of the brain in autism spectrum disorders (ASD). Despite previous findings of abnormalities in the brain in ASD, results have been fairly inconsistent and the affected brain areas and connections varied. Therefore, a firm neurobiological etiology of ASD has been rather elusive, and the need to find reliable neural signatures for the disorder has been paramount. Multimodal neuroimaging approach may provide a novel and valuable window of opportunity in this regard as such investigations may provide a global characterization of the brain in ASD. The current study utilizes proton magnetic resonance spectroscopy (1H-MRS), diffusion tensor imaging (DTI), and functional MRI (fMRI) to examine the brain in high-functioning adults with ASD.

Objectives: To determine brain metabolite levels and white matter integrity, and their relationship to brain functioning in high-functioning adults with ASD.

Methods: Eighteen high-functioning adults with ASD and 18 typically developing (TD) control participants took part in this study.1H-MRS, DTI,

and fMRI data were acquired using a 3T Siemens Allegra scanner. Spectra for N-acetylaspartate (NAA), choline (Ch), glutamate/glutamine (Glx) and creatine (Cr) were acquired from two regions of interest, the dorsal anterior cingulate cortex (dACC) and the posterior cingulate cortex/precuneus (PCC). DTI data were collected using a single shot, spin echo sequence in 46 orthogonal directions. fMRI data were acquired during a task that assess the processing of emotional body language.

Results: The main results are as follows: (1) Significantly reduced NAA/Cr in ASD participants compared to TD peers in the dACC [$t(34)=3.09$, $p=0.004$]. A marginally significant lower level of Glx/Cr in ASD relative to TD participants in the dACC [$t(34)=1.91$, $p=0.06$]. There were no significant differences in any of the neurochemicals for the PCC voxel; (2) A significant positive relationship was found between NAA/Cr level in dACC and brain activity in dACC during emotional body language processing, with greater metabolite concentration predicting greater activation in that region; and (3) The DTI data showed significantly lower fractional anisotropy (FA) in right cingulum bundle, especially along several anterior nodes, in ASD adults compared to TD peers. Other tracts that showed reduced FA in ASD include the bilateral inferior frontal occipital fasciculus, left superior longitudinal fasciculus, right inferior longitudinal fasciculus, and right uncinate fasciculus.

Conclusions: Differences in NAA/Cr level in the dACC are in line with the findings of a recent study (Fujii et al., 2010), and indicative of possible alterations in neuronal and axonal health in this region in ASD adults. The correlation between 1H-MRS findings and fMRI based brain activity during a social cognition task suggest and the importance of neuronal health in brain functioning. Affected white matter tracts in ASD adults point to potential problems of brain connectivity and myelination in ASD. Converging findings from this multimodal neuroimaging study provide evidence for the pathobiology of ASD brain at multiple (neurochemical, functional, and structural) levels.

**155.031 31** Structural Anatomy of the Social Brain in Autism: An Activation Likelihood Meta-Analysis. T. DeRamus* and R. K. Kana, *University of Alabama at Birmingham*

Background: Voxel-based morphometry (VBM) studies of autism, that measure cortical volume and thickness, have provided mixed and occasionally conflicting results. This may in part be due to a large extent of heterogeneity among the study samples. Nevertheless, reports of grey and white matter volumetric differences in regions associated with social cognition and executive function have been relatively consistent. The goal of this study is to characterize the anatomical differences within social brain regions in autism using activation likelihood estimation (ALE) meta-analysis of structural morphometry studies in autism.

Objectives: To consolidate the patterns of anatomical alterations in the brains of individuals with ASD through a comprehensive meta-analysis of structural neuroimaging studies.

Methods: Twenty-three structural neuroimaging studies of autism that met the following inclusion criteria were considered for this meta-analysis: 1) whole-brain VBM method of analyses; 2) participants with IQs > 70; and 3) participants had no comorbid conditions. The foci of results from increased and decreased grey and white matter contrasts between ASD and control participants from these studies were used to conduct ALE using GingerALE 2.3 (Laird et al., 2005; Laird, Lancaster, & Fox., 2008; Turkeltaub et al., 2002). Two analyses of pooled grey and white matter, one of increased and one of decreased, were conducted and reported at a false discovery rate (FDR) of 0.05 with a minimum cluster size of 200mm3 for significant clusters as the threshold (Turkeltaub, 2012). Maxima results were verified using the 2mm MNI 152 brain template in FSL (Smith et al., 2004; Woolrich et al., 2009; Jenkinson et al., 2012).

Results: Clusters of increased cortical matter in ASD, relative to controls, were found in the right medial prefrontal cortex (MPFC), premotor cortex, left frontal pole, superior frontal gyrus (SFG), superior temporal gyrus (STG), and fusiform gyrus. Significant clusters of decreased cortical matter in ASD relative to controls were found in the left anterior cingulate cortex (ACC), inferior occipital gyrus (IOG), angular, and postcentral gyrus. Increases were also found in subcortical structures like the left caudate and putamen and right cerebellar vermis. Other structures that showed group differences included the right

amygdala and the white matter underlying the ACC.

Conclusions: Significant alterations in grey and white matter were primarily found in clusters within areas (e.g., ACC, MPFC, Amygdala, STG, Caudate, Fusiform, Putamen, and Cerebellum) associated with social and executive processing, both of which are impaired in ASD. These findings provide further insight into functional deficits within social brain areas in ASD by providing evidence of the underlying anatomical abnormalities. This meta-analysis, which strictly controlled for IQ and comorbid conditions, to our knowledge is the first one to apply such stringent criteria to morphometric meta-analysis in autism.

**155.032 32** Neuroanatomical Signatures of Autism. D. Yang*, R. J. Jou and K. A. Pelphrey, *Yale University*

**Background**: In an fMRI study of children with autism spectrum disorder (ASD), unaffected siblings of children with ASD (US), and typically developing children (TD), Kaiser and colleagues (2010) identified three different kinds of biomarkers: (a) state regions: functionally weaker in ASD (relative to TD and US), reflecting the state of having ASD; (b) trait regions: functionally weaker in both ASD and US (relative to TD), reflecting the underlying genetic vulnerability for ASD; and (c) compensatory regions: functionally stronger in US (relative to ASD and TD), suggesting a pathway by which US might avoid developing ASD. It remains unclear how these neurofunctional biomarkers might map onto neuroanatomical characteristics in ASD.

**Objectives**: We aimed at elucidating the neuroanatomical biomarkers of autism by comparing and contrasting the cortical thickness among ASD, TD, and US in a large sample of children with groups rigorously matched on sex, age, and IQ.

**Methods**: Study participants included 209 children (age: 4-12 years old), including 100 children with ASD (25 females and 75 males), 70 TD children (28 females and 42 males), and 39 US children (17 females and 22 males). Expert clinical diagnosis of ASD was confirmed via the ADOS and ADI-R. For every participant, a high-resolution, T1-weighted MPRAGE structural scan was acquired using a 3-Tesla Siemens Tim Trio scanner. Cortical reconstruction was performed using FreeSurfer 5.1.0. We sought to identify (a) state regions, where the cortical thickness in ASD was thinner than both TD and US; (b) trait regions, where cortical thickness in both ASD and US children is thinner than TD children; and (c) compensatory regions, where cortical thickness in US is thicker than both children with ASD and TD children. To correct for multiple comparisons, we employed a Monte Carlo simulation (cluster analysis) with an *a priori* threshold of $p < .05$ for whole-brain correction.

**Results**: Trait regions were not apparent following whole-brain correction. State and compensatory regions were localized mainly to the temporal and frontal lobes as well as the insular cortex. Among the state regions, the cortical thickness of the right posterior superior temporal sulcus (pSTS) and that of the right lateral orbitofrontal cortex were highly negatively correlated with ADOS module 3 social affect scores ($ps < .01$, corrected), suggesting that cortical thickness in these regions is a sensitive biomarker of social-communication dysfunction in ASD.

**Conclusions**: We generally replicated the prior functional MRI findings using a large structural MRI dataset while identifying additional state and compensatory regions, providing convergent evidence for the neural signatures of ASD originally identified by Kaiser et al. (2010). Future studies are warranted to further characterize these neurobiological signatures using other imaging modalities, including diffusion MRI. Full characterization of the neural signatures of ASD is essential to guide future work aimed at elucidating the neural-systems-level pathophysiology of ASD and developing guidance for treatment.

**155.033 33** Study of 38 Brain Regions Demonstrates Alterations Restricted Mainly to Structures Involved in Repetitive Behaviors and Social Deficits. J. Wegiel*[1], M. J. Flory[2], I. Kuchna[2], K. Nowicki[3], S. Y. Ma[3], H. Imaki[3], J. Wegiel[4], I. L. Cohen[3], E. London[2], W. T. Brown[5] and T. Wisniewski[6], (1)*New York State Institute for Basic Research*, (2)*NYS Institute for Basic Research in Developmental Disabilities*, (3)*New York State Institute for Basic Research in Developmental Disabilities*, (4)*The College Of Staten Island (CUNY)*, (5)*NYS Institute for Basic Research in DD*, (6)*New York University School of Medicine*

Background: Individual brain structures have distinct developmental profiles during brain development (Caviness et al 1996, Herbert et al

2003, Piven et al 1996). MRI and postmortem studies indicate that autism is associated with selective alterations of the developmental profiles of some brain structures.

Objectives: The aim of our study was to detect the global pattern of developmental abnormalities and to establish whether the function of developmentally modified structures matched the autism diagnostic behavioral alterations. Detection of a global pattern required examination of 38 brain cytoarchitectonic subdivisions, including 15 brain structures and their 23 subdivisions, representing subcortical and cortical structures, cerebellum and brainstem in 4- to 60-year-old autistic and control subjects.

Methods: To achieve this aim, 14 autistic and 14 age-matched controls were selected on the basis of clinical inclusion and neuropathological exclusion criteria. The Cavalieri method was applied to estimate brain subdivision volumes. The numerical density and total number of neurons per region of interest were estimated using the MicroBrightfield software.

Results: Application of the Cavalieri method revealed significant volume alterations in the autism group in the caudate nucleus and nucleus accumbens only. In the autistic group, the caudate nucleus volume was larger by 22% (2,107 $mm^3$) than in the control cohort (1,727 $mm^3$; $p < 0.026$). The nucleus accumbens was larger in the autistic group by 34% (244 $mm^3$) compared to in the control cohort (182 $mm^3$; $p < 0.026$). The observed pattern of neuronal number changes in the striatum does not support the concept that there is increased volume of the brain subdivisions due to impaired neuronal pruning resulting in an increase in the number of neurons. In contrast, the numerical density of neurons in the autistic putamen was 13% less than in control subjects (24,302/$mm^3$ and 27,838/$mm^3$, respectively; $p < 0.04$), and of neurons in the autistic nucleus accumbens was 15% less (34,258/$mm^3$ versus 40,459/$mm^3$; $p < 0.01$). The numerical density of neurons was also reduced in two other striatal subdivisions, the caudate nucleus (-7%) and the globus pallidus (-10%), but these differences did not reach significance. The 12% reduction detected in the numerical density of neurons in the lateral nucleus of the amygdala in autistic subjects (24,282/$mm^3$) in comparison to controls (27,632/$mm^3$; $p < 0.006$) and the 17% reduction in the total number of neurons resemble the selective 13% reduction of the number of neurons in the lateral nucleus reported by Schumann and Amaral (2006).

Conclusions: This postmortem study of 38 brain subdivisions demonstrates that in autism, alterations in the number of neurons and in the volume of brain structures are limited to a few brain regions, including the nuclei of the striatum and amygdala. These findings support and expand MRI data (Sears at al 1994, 1999; Hollander et al 2005) and indicate that increased striatal volume and decreased number of neurons likely contribute to restricted, repetitive, and stereotypical behaviors. The results also support studies by Schumann and Amaral (2006) that showed a link between alterations in the amygdala and social deficits.

**155.034 34** Behavioral and Neural Basis of Anomalous Motor Learning in Autism. M. K. Marko*[1], D. Crocetti[2], R. Shadmehr[1] and S. H. Mostofsky[2], (1)*Johns Hopkins University*, (2)*Kennedy Krieger Institute*

Background: Theory suggests that motor learning either underlies or parallels learning of social and communication skills, deficits of which are at the core of autism spectrum disorder (ASD). Children with ASD demonstrate both hyper- and hypo-sensitivity to sensory stimuli, as well as generalized motor impairments. Specifically, studies of motor learning have suggested an over-reliance on proprioception. The cerebellum, which plays a key role in motor learning, is frequently implicated in ASD for abnormalities on both a cellular and gross level. As such, cerebellar structure may be related to patterns of sensorimotor learning in children with ASD.

Objectives: Quantify how children with ASD learn from different sensory modalities of error and relate this to gross cerebellar anatomy.

Methods: Forty children, ages 8-12, participated in the task: 20 with ASD and 20 typically developing (TD) controls. Groups were matched for gender (Fischer's exact test, $p=0.41$), age ($t(38)=2.0$, $p=0.18$), intelligence (WISC-IV Perceptual Reasoning Index) ($t(38)= -1.51$, $p=0.14$), and Edinburgh Handedness score ($t(38)=-0.64$, $p=0.52$). For the psychophysical study, children participated in a reaching task in which their movements were given either a visual or proprioceptive perturbation during the course

of their reach. Sensitivity to these errors was measured as the relative compensation that occurred on the subsequent trial. Children also participated in an imaging study including a high resolution T1-weighted image using a 3T Philips Achieva. The resulting image was parcellated using an automatic protocol to produce regional volumes, according to the atlas in Schmahmann (Schmahmann et. al. 2000).

Results: We found that children with ASD showed an increased sensitivity to proprioceptive error (repeated measures ANOVA, significant effect of group ($F(1,38)=5.0$, $p=0.032$), field ($F(1.1,40.4)=8.8$,$p=0.004$) and group by field interaction ($F(1.1,40.4)=4.3$, $p=0.043$)) and a decreased sensitivity to visual error (repeated measures ANOVA, significant effect of group ($F(1,38)=6.4$,$p=0.015$), visual gain ($F(1.1,42.0)=5.2$,$p=0.024$), but no significant interaction ($F(1.1,42.0)=1.7$,$p=0.202$)) when compared to TD controls. Further, the sensitivity to error in each modality was anti-correlated ($R^2=0.56$, $p < 0.001$), such that as one expressed greater sensitivity to proprioceptive error, they showed less sensitivity to visual error, with the ASD group showing a cluster towards proprioceptive reliance. Using a generalized linear model (GLM), we related this proprioceptive bias to the volume of the right anterior lobe and right lobule VI in the cerebellum. The GLM had a significant omnibus result (likelihood ratio $\chi^2(5)=13.6$, $p=0.018$), compared to an intercept only model. Further, we found a significant main effect of lobule VI volume (Wald $\chi^2= 5.125$, $p=0.024$), as well as a significant group by lobule VI volume interaction (Wald $\chi^2= 6.495$, $p=0.011$) on the proprioceptive bias.

Conclusions: Our results demonstrate that children with ASD show an abnormal pattern of motor learning with a bias towards proprioceptive rather than visual feedback, and that this pattern is related to the volume of specific regions of the cerebellum. The nature of this abnormality in motor learning may underlie deficits in acquiring social and communication skills in autism and could provide opportunities for developing novel therapies for improving motor, social, and communicative skills in people with ASD.

**155.035 35** White and Grey Matter Abnormalities and Cognitive Functioning in Autism Spectrum Disorders. S. V. Huemer*[1], F. Kruggel[2], V. Mann[2] and J. Gehricke[2], (1)*University of CA - Irvine*, (2)*University of California, Irvine*

**Background:**

Atypical brain growth in ASD has been linked to functional underconnectivity and the autism phenotype. Imaging research indicates that white matter abnormalities in autism spectrum disorder (ASD) affect long-distance neural connections and entire neural networks, mostly those of higher-order functioning. More studies are needed to better define the characteristics of the neural abnormalities and their association with cognitive deficits in ASD.

**Objectives:**

We planned to examine neuroanatomical differences between ASD adolescents and typical controls and wanted to probe whether the neuroanatomical differences in ASD are associated with cognitive functioning.

**Methods:**

We used structural magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) to compare the neuroanatomy of 20 adolescents with ASD and 10 typical controls. We applied Voxel Based Morphometry (VBM) for a between-group comparison of the local concentration of grey and white matter, Tensor Based Morphometry (TBM) to detect group-related differences in the shape of brain regions, and DTI to quantify and compare differences in white matter (WM) microstructure. Cognitive function was measured by using the *Peabody Picture Vocabulary Test Third Edition (PPVT-III).*

**Results:**

*VBM results*

The ASD group showed a **significantly lower grey matter concentration (GMC)** in inferior portions of the left frontal lobe, most notably the operculum, which includes Brodmann area 44 (Broca's), the right superior temporal gyrus, responsible for auditory and language processing, and the left anterior cingulate, a processing switchboard implicated in learning and problem solving. The ASD group showed **a significantly higher white matter concentration (WMC)** in the upper portions of the frontal lobe on both

sides and the middle temporal and superior temporal gyrus on the right. Activity across the frontotemporal network has been shown to be desynchronized in ASD. **Significantly lower WMC** was found in the mid portions of the right frontal lobe, the left cingulate gyrus, and the right postcentral gyrus, which receives the bulk of thalamocortical projections from sensory input fields.

*TBM results*

**Group-related shape differences** detected significant shrinkage and expansionin the ASD group in regions that are in over-projection with the uncinate fasciculus, which connects parts of the limbic system of the temporal lobe to parts of the frontal lobe, and a significant shrinkage along the inferior temporal gyrus and the fusiform gyrus on the left side, an area implicated in face and word recognition.

*PVVT-III as independent variable*

We used the percentile scores from the PPVT-III instead of group designation and found a negative correlation between low scores and significantly increased GMC in the parahippocampal gyrus, along with an increased WMC and increased fractional anisotropy (FA) in the temporal lobe. In the lower scoring subjects, several regions with increased WM density were found along the uncinate fasciculus and the left and right arcuate fasciculus, which connects Broca's with Wernicke's.

**Conclusions:**

Our results point to significant disturbances in major neural pathways in ASD. Most interestingly, our study indicates that the neurological profile of high functioning ASD subjects lies on a continuum with typically developing controls rather than clustering with that of ASD subjects with more severe cognitive impairments.

**155.036 36** Are Autistic Traits in the General Population Related to Global and Regional Differences in Brain Structure?. P. C. M. Koolschijn*, H. M. Geurts, A. R. Van der Leij and H. S. Scholte, *University of Amsterdam*

**Background:**

There is accumulating evidence that autistic traits in the general population lie on a continuum, with clinical ASD representing the extreme end of this distribution. Individual differences in autism-spectrum quotient (AQ) have been shown to predict differences in performance on behavioral tasks that are impaired in ASD. Yet it remains unknown if individual differences in AQ also relate to brain anatomical measures. It could be argued that biological mechanisms associated with clinical ASD may also underpin variation in autistic-like traits within the general population. Here, we want to elucidate the possible effects of autistic traits on various indices of brain structure in the general population and compare the results with neuroanatomical differences reported in ASD.

**Objectives:**
To address whether AQ scores in the general population are related to structural variation in global or local gray matter volume, thickness and surface area.

**Methods:**
All healthy individuals completed the abbreviated version of the AQ questionnaire (28 items). High-resolution T1 anatomical MRI scans were acquired from 508 healthy individuals. We performed a quantitative cross-validation on structural brain indices by creating two independent stratified groups based on age, sex, and level of education: Group1: N=204 (105 Males, Mean age=22.85, SD=1.7, Mean AQ=55.6, SD=9, range=33-80); Group2: N=304 (155 Males, Mean age=22.82, SD=1.7, Mean AQ=57.1, SD=8.7, range=32-91). To assess global differences in brain structure, FreeSurfer was used to derive cortical thickness and surface area measures. Regional volumes were assessed with VBM. To examine the relationship with behavior, correlations between structural brain indices and AQ were calculated taking age, sex and handedness into account.

**Results:**
Here we present preliminary results based on Group1, using a standard cross-sectional approach including correction for multiple comparisons.
No significant associations were found between AQ scores and cortical thickness or surface area in Group1 (FDR, $p<.05$, >100 vertices) or on regional brain volumes using permutation-based non-parametric testing.

**Conclusions:**
The first preliminary analyses do not indicate that

ASD symptom severity is related to gray matter volume, thickness or surface area in healhty young adults. Hence, it could well be that the relationships observed in clinical populations are unique for those with an actual disorder instead of being of relevance for those with mild ASD symptoms in the general population. We are currently pursuing the actual cross-validation between groups and expect to present the results on May 2014.

## 156 Early Development

**156.037 37** Comparison of the Clinical Profiles of 1-Year Olds and 2-Year Olds with Autism Spectrum Disorders. R. E. Aiello*[1], K. Jenkins[2], Z. Warren[3] and C. R. Newsom[3], (1)*Vanderbilt University Medical Center*, (2)*Tennessee State University*, (3)*Vanderbilt University*

Background: Accurate, stable diagnosis of ASD may be possible within community settings during the second year of life for some children (Corsello et al., 2012; Guthrie et al., 2012), and young children with ASD receiving early behavioral intervention demonstrate substantial gains in functioning (Dawson et al., 2010, 2012; Warren et al., 2011). Numerous screening initiatives (AAP, CDC Act Early) have pushed for identification prior to age two. However, CDC figures suggest a majority of individuals with ASD are not diagnosed until after age 3. To date, few studies outside of high-risk sibling protocols have characterized the developmental profiles of toddlers with ASD in the 1 and 2-year age range. It remains unclear whether children identified before age two evidence more concerning clinical profiles (e.g., lower cognitive abilities, severe impairments of adaptive functioning, higher levels of ASD symptoms) than children identified at later ages. Understanding such differences has implications for programs targeting universal screening and very early diagnosis.

Objectives: This project explored the developmental profiles of toddlers diagnosed with ASD in the 2nd year of life in comparison to children diagnosed in the 3rd year of life in a well-characterized university clinical research database. We examined whether younger children evidenced profiles of more significant delays and impairments.

Methods: Participants included children seen through university-affiliated developmental clinics as well as children participating in a variety of research protocols (e.g., genetic collections, infant sibling studies, intervention protocols). 488 children below the age of 36 months ($n$ = 63 <24 months; $n$ = 425 between 24 and 35 months) were included in the sample. All children were newly diagnosed with ASD. Diagnostic measures included the MSEL, ADOS, and VABS. Child demographics including gender, rural/urban setting, and sibling status via caregiver report were also utilized.

Results: A series of preliminary independent samples t-tests were conducted to compare differences in developmental profiles for children below 24 months of age and children between 24-35 months of age. There was a statistically significant difference in overall performance of the MSEL composite for children with ASD diagnosed before 24 months of age ($M$ = 61.4, $SD$ = 13.1) compared to those diagnosed between 24-35 months of age ($M$ =57.7, $SD$ =14.8) scores, $t(475) = 2.00$, $p < .05$. No differences were obtained for the VABS Composite scores; however, differences were observed within the VABS Socialization domain between the below 24 months group ($M$ = 73.4, $SD$ = 6.42) and the 24-35 months group ($M$ = 68.8, $SD$ = 8.43), $t(471) = 2.31$, $p < .05$. No differences were observed in ADOS Comparison scores between the two groups.

Conclusions: Preliminary results suggest that children identified before 24 months of age do not evidence patterns of more pronounced delay than children diagnosed after two. In fact, children identified before 2 demonstrated higher cognitive and adaptive behavior scores. This finding suggests that early identification efforts aimed at identifying very young children are not simply identifying children with more severe delays.

**156.038 38** Learning from Exploration: Manual Exploration Strategies in Infants with and without ASD. K. Libertus* and J. M. Iverson, *University of Pittsburgh*

Background: Object exploration skills are critical for learning about the physical and social world. A growing number of studies suggest that infants' motor and exploration skills may influence development across domains, including perceptual and social-cognitive development (e.g., Libertus & Needham, 2010, 2011; Soska, Adolph, & Johnson, 2010). Further, atypical or delayed motor skills are commonly observed in children and adults with Autism Spectrum Disorders (ASD) and may manifest early in development (Bhat, Landa, & Galloway, 2011). Infants at high risk for ASD have

been reported to show delayed postural control and gross motor skills (Flanagan, Landa, Bhat, & Bauman, 2012; Nickel, Thatcher, Keller, Wozniak, & Iverson, 2013). Early motor delays may affect object exploration strategies in infants later diagnosed with ASD and interfere with their learning about the physical and social world.

Objectives: Characterize manual exploration strategies in infants later diagnosed with ASD to inform understanding of developmental etiology and early intervention approaches.

Methods: Manual exploration strategies are observed in a total of 50 infants (20 low-risk (LR) infants without ASD, 20 high-risk (HR) infants without ASD, and 10 infants diagnosed with ASD at age 36 months). As part of a larger longitudinal study, infants were videotaped at home for 45 min at six and ten months of age. Manual exploration analyses focus on infants' behavior during a 1 min object exploration task using a toy rattle.

Results: Proportions of time infants engaged in active mouthing (out of all mouthing), one-handed exploration, and object shaking (out of all touching) were analyzed. Analyses to date indicate that at age six months, ASD infants show less active mouthing behavior than LR infants ($M_{ASD}$ = 46.91%, $M_{LR}$ = 80.57%), but more one-handed exploration ($M_{ASD}$ = 62.30%, $M_{LR}$ = 36.19%,). High-risk infants without ASD fall in-between the LR and ASD groups on both measures ($M_{Mouthing}$ = 56.08%, $M_{One\text{-}hand}$ = 45.82%). By age ten months, LR infants increase their functional exploration of the toy rattle by showing more shaking behavior ($M_{6m}$ = 14.27%; $M_{10m}$ = 24.39%). In contrast, ASD infants show no such increase from six to ten months of age ($M_{6m}$ = 16.33%; $M_{10m}$ = 14.46%). High-risk infants without ASD show a small increase in shaking over the same time-period ($M_{6m}$ = 11.23%; $M_{10m}$ = 17.32%).

Conclusions: Object exploration strategies differ between infants subsequently diagnosed with ASD and typically developing infants. Infants later diagnosed with ASD seem to provide themselves with fewer opportunities to learn about critical object features such as texture or function by engaging less in active mouthing and shaking behaviors. Further, one-handed grasping preferences may be counterproductive and hinder overall grasping success in infancy. In agreement with recent findings (Nickel et al., 2013), one-handed grasping also suggest relative postural instability in infants later diagnosed with ASD as the second hand might be needed to stabilize the body during exploration. These preliminary results indicate that early fine motor skills should be closely observed in infants at high genetic risk for ASD and that motor training should be included in early intervention approaches.

**156.039 39** Do Two-Year Olds with ASD Orient to Sounds They Do Not Share. L. B. Adamson*, D. Robins, R. Bakeman, A. M. Kellerman and A. A. Hasni, *Georgia State University*

**Background:** There have been several demonstrations of impaired orientation to brief auditory stimuli in children with autism spectrum disorder (ASD), particularly to speech and social stimuli, and of impaired initiation of joint attention. However, we are not aware of studies that detail the relation between alerting and orientating to a sound and initiating joint attention to the sound. Initiating joint attention to a sound is one part of the process of auditory joint engagement—a child's active sharing of sounds during parent-child interactions—that we anticipate is impaired in young children with ASD in ways that may have significant implications for communication and language development.

**Objectives:** The current study sought to test the hypothesis that young children with ASD are less apt than other children to issue bids to share sounds even when they clearly alert and attend to them.

**Methods:** The Screening Tool for Autism in Toddlers and Young Children (STAT; Stone & Ousley, 1997; Stone et al., 2004) was used to observe 30 24-month-olds who were subsequently diagnosed with ASD, 30 diagnosed with a non-ASD developmental disorder (DD), and 30 who were typically developing (TD). One item (the noisemaker task) assessed whether the child initiated joint attention with an experimenter when she briefly activated a clicker hidden beneath the table (a sound that Orekhova et al., 2012, recently reported has atypical neurofunctional correlates in ASD). Videorecords of the child's alerting, orienting, and bids to initiate joint attention were reliably coded.

**Results:** Most children (29 of the 30 with DD, 29 of the 30 TD, and 24 of the 30 diagnosed with

ASD) both alerted and oriented to the sound. Of those, children in the DD and TD groups were 4 times more likely to initiate joint attention to the sound than children in the ASD group (20, 23, and 10 initiated; odds ratio = 4.01, 95% CIs = 1.47–10.9, $p$ = .007).

**Conclusions:** These findings demonstrate that although young children with ASD are almost as likely to alert and orient to a sound as other children, they are significantly less likely to attempt to spontaneously share that sound with an adult. These results underscore the importance of investigating variations in responses to sounds and their integration into joint engagement. Moreover, they help motivate research efforts that systematically expand the study of auditory joint engagement to include a variety of sounds, including speech, and a broader range of child reactions, including how they respond to adult bids for auditory joint engagement.

**156.040 40** Early Identification of Toddlers with Autism Spectrum Disorder at 18-24 Months of Age By the Screening Tools for Autism in Two-Year-Olds Taiwan Version (T-STAT). C. C. Wu*[1], C. H. Chiang[2] and Y. M. Hou[3], (1)*Kaohsiung Medical University*, (2)*National Chengchi University*, (3)*Department of Psychiatry, Ditmanson Medical Foundation Chia-Yi Hospital*

Background: Autism spectrum disorder (ASD) is characterized by impaired social interaction and communication, as well as restricted and repetitive behavior and interest. Over past decade, some studies reported that prevalence of ASD has increased markedly. Previous studies reported that early intervention improved outcomes for toddlers with ASD (Dawson et al., 2010; Landa et al., 2011). The benefits of early intervention highlighted the importance of earlier identification of toddlers with ASD. The American Academy of Pediatrics (AAP) has recommended that all infants receive universal screening for autism less than 24 months old (Johnson et al., 2007). However, the diagnosis of ASD is still often delayed because diverse factors, for example, limitations in utility of screening instruments.

Objectives: There are few level 2 screening tools to distinguish ASD from other developmental disorders for toddlers before 24 months. It would weaken work of early diagnosis and early intervention for children with ASD. Therefore, the current research, there are two studies to test utility of using the Screening Tools for Autism in Two-Year-Olds, Taiwan version (T-STAT) (Chiang et al., 2012, 2013) for toddlers with ASD from 18 to 24 months of age.

Methods: The T-STAT is a 12 items interactive autism-specific screening tool, including four behavioral domains: play (2 items), requesting (2 items), joint attention (4 items) and imitation (4 items). Within both play and requesting, if a toddler fails one item, he would receive a score of 0.50. Within both joint attention and imitation, if a toddler fails one item, he would receive a score of 0.25. The scores of four domains are from 0 to 1. The scores of four domains are summed, obtaining a total T-STAT scores which from 0 to 4.

Results: Study 1, there are 30 toddlers from 18 to 24 months of age, including 15 toddlers with ASD and 15 toddlers with developmental delayed (DD). Using signal detection procedures, the optimal cutoff of the total T-STAT score was decided. The results revealed that 2.25 or 2.50 was the best cutoff. Using the 2.25 of total T-STAT score as cutoff, the sensitivity and specificity are .93 and .93, respectively. In addition, positive predicative value (PPV) is .93 and negative predicative value (NPV) is .93. Using the 2.50 of total T-STAT score as cutoff, the sensitivity and specificity are .87 and .93, respectively. In addition, PPV is .93 and NPV is .88. Study 2, there are 70 toddlers from 18 to 24 months of age, including 33 toddlers with ASD and 37 toddlers with DD. Using the 2.25 as cutoff, the sensitivity and specificity are .91 and .89, respectively. In addition, PPV is .88 and NPV is .92. Using the 2.50 as cutoff, the sensitivity and specificity are .91 and .95, respectively. In addition, PPV is .94 and NPV is .95.

Conclusions: The results of this current research showed that the T-STAT is a promising good tool to differentiate the toddlers with ASD and toddlers with DD from 18 to 24 months of age.

**156.041 41** Emergence of Social Engagement in Infants at High and Low Risk for ASD As Indexed By Cry. Y. Stern*, S. Ghai, A. Klin and G. J. Ramsay, *Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*

Background: Early infant cry is reflexive in nature, and initially reflects the internal condition of the infant. Yet as the infant develops within the first months of life, cry gradually evolves into a volitional prelinguistic vocalization used to negotiate social interactions, and begins to reflect

the emergence of socialization. Previous work has demonstrated that acoustic and durational features of cries in early infancy determine the nature of parental perception of cry and latency of response to cry, in typical development and in developmental disorders other than autism. As studies have shown that cry of infants at high genetic risk for ASD and toddlers with ASD have atypical cry characteristics, it is important to understand whether these atypicalities affect the quality of emergent social engagement between infants at risk for ASD and their caregivers.

Objectives: The focus of this study was to determine whether the function of cry is disordered in infants at high genetic risk for ASD, relative to those at low genetic risk for ASD, before signs of deficits in social communication apparent in speech may emerge. As cry becomes an infant's means of initiating and responding to social interaction in infancy, the goal of the project was to investigate the efficacy of cry in negotiating social interactions in these high-risk infants. We explore the hypothesis that high-risk infant cries evoke maternal responses that less effectively capitalize on the social value of cry, compared to cries of low-risk infants.

Methods: As part of a larger ongoing NIH Autism Center of Excellence, tracking vocal development in 230 high-risk infants (with older siblings already diagnosed with autism) and 100 low-risk infants (with no family history of autism), digital audio recording devices (LENA Foundation) were sent to families' homes monthly, beginning at 1-2 months, for the purpose of making day-long, naturalistic recordings of infants' vocalizations. In this study, we focused on an exhaustive analysis of 2 high-risk infants and 2 low-risk infants, at three time points between 1 and 6 months. We labeled and segmented cries and the corresponding maternal response to these cries using a customized coding scheme. We then evaluated the nature of infant cry and maternal response to cry.

Results: The quality of response to cry differed perceptually between the high-risk and low-risk infants. Maternal response to high-risk infant cry was less sustained and less varied than response to low-risk infant cry. Further, while cry was a definite means of communication for several of the low-risk infants by 6 months, one of the high-risk infants hardly cried at all throughout the 2-month recording and systematically failed to evoke differential maternal responses.

Conclusions: Systematic atypicalities in cry at different stages of development are likely to provoke sustained changes in interactional style between parent and child. The adaptive function of cry to serve as a platform for social engagement between infant and caretaker may be weakened in interactions between mothers and their high-risk infants.

**156.042 42** The Relation Between Infant Social Engagement and Maternal Behavior in Infants at High-Risk for Autism Spectrum Disorder. C. M. Harker*, T. P. Nguyen, L. V. Ibanez and W. L. Stone, *University of Washington*

**Background:**

Early parent-child interactions play an influential role in shaping children's social and communicative development, and these interactions may have an even greater impact on the development of children at high risk for developmental challenges (e.g., Landry et al., 2006). One such high risk group is infant siblings of children diagnosed with Autism Spectrum Disorder (ASD; HR-infants), who are at increased risk of developing ASD compared to infant siblings of typically developing children (LR-infants; Georgiades et al., 2012). It has been theorized that early impairments associated with ASD may affect the quality of parent-child interactions, which over time may lead to an increasingly atypical social developmental trajectory (Dawson, 2008). Social smiling is one behavior known to play a role in initiating and maintaining early parent-child interactions (Messinger & Fogel, 2007), and this behavior has been found to be reduced in HR-infants (Cassel et al., 2007). There is a lack of research on how infant social smiling may affect maternal behaviors in HR-infants, and in turn, how maternal behaviors may influence infant social smiling. It has been proposed that maternal behaviors that promote engagement and reciprocity may attenuate ASD symptom development over time for HR-infants (Dawson, 2008). Two parenting behaviors that have been identified as influential are maternal responsiveness and directiveness (Mahoney, 2008). Emerging research suggests that mothers of HR-infants display less responsive and more directive behavior when compared with mothers of LR-infants (Wan et al., 2012).

**Objectives:**

The objectives of this study were to examine: (1) Whether growth in infant social smiling between 9 and 18 months predicts maternal responsiveness and directiveness at 18 months; and (2) Whether maternal responsiveness and directiveness at 9 months predict growth in infant social smiling between 9 and 18 months; and (3) Whether there are differences in these relationships between HR-infants and LR-infants.

**Methods:**

Our total sample included 29 mother-infant dyads, 19 HR-infants (10 male) and 10 LR-infants (6 male). Observations of maternal and infant behaviors were coded during a 5-minute free play interaction. Infant social engagement was operationalized as the frequency of social smiling during this interaction. Maternal responsiveness and directiveness were measured using a modified version of the Maternal Behavior Rating Scale (Mahoney, 2008); ICCs ranged from .72-.96.

**Results:**

Four hierarchical regressions were conducted to examine the association between infant and maternal behaviors and risk group status as a moderator. Maternal directiveness ($\beta$=-.67, p=.01) and risk group status ($\beta$=-.45, p=.01) were independent predictors of growth in infant social smiling, with a trend for moderation ($\beta$=.41, p=.08). Growth in infant social smiling did not predict maternal responsiveness or directiveness at 18 months, and maternal responsiveness at 9 months did not predict growth in infant social smiling; there was no moderation.

**Conclusions:**

Higher levels of maternal directiveness were associated with slower growth in infant social smiling. The trend for moderation suggests a stronger association between directiveness and growth in social smiling for HR- infants relative to LR-infants. Data coding is ongoing.

**156.043 43** Biochemical Assessment of Circadian Processes in ASD. G. M. Anderson*[1], S. Samanta[2], T. Brand[3] and K. Chawarska[1], (1)*Yale University School of Medicine*, (2)*Yale Univ, Sch. of Medicine*, (3)*Yale Univ. Sch. Medicine*

Background: The pineal hormone melatonin (MEL) is secreted with a marked day-night rhythm and it plays a crucial role in circadian rhythms. MEL also has powerful antioxidant properties. Studies in school-age children, adolescents and young adults have reported lower group mean production of melatonin in ASD.

Objectives: We wished to examine daytime and nighttime production of MEL, as well as other diurnally varying neurohormones, in younger ASD and typically developing individuals in order to understand better this apparent deficit and to assess the potential utility of the measure in screening.

Methods: Melatonin sulfate, norepinephrine, epinephrine, cortisol and creatinine were measured in methanolic extracts of daytime and overnight diapers obtained from toddlers ages 18-36 months. ASD subjects received an extensive behavioral assessment and caregivers completed a questionnaire asking about sleep and gastrointestinal related behaviors and problems.

Results: Diapers have been obtained from 53 typically individuals and a similar number of ASD subjects. Analysis of diaper extracts for the neurohormones has been successful and data analysis is ongoing.

Conclusions: Collection and extraction of daytime and overnight diapers obtained from toddlers with ASD provides a feasible approach to the study of circadian rhythms in younger individuals with ASD. The completed data analysis will indicate whether lower production of melatonin is also found in younger individuals with ASD and will examine the specifity of potential alterations in diurnally vary neurohormones.

**156.044 44** Infant Emotional Responsiveness and Autism Risk. N. M. McDonald*[1], B. L. Lambert[2], W. Mattson[2] and D. S. Messinger[2], (1)*Yale School of Medicine*, (2)*University of Miami*

Background: Emotional responsiveness is important for maintaining positive interactions between social partners. Individuals with autism spectrum disorder (ASD) show impairments in emotional responsiveness. A crucial component of emotional responsiveness is responsive social smiling, in which one social partner's smile appears to be contingent on the other's smile. In typically developing children, responsive social smiling develops within the first six months of life; however, less is known about early smiling

behaviors, particularly responsive social smiling, in infants at elevated risk for ASD.

Objectives: We utilized a micro-coding approach to investigate the relation between smiling during early parent-infant interactions and later ASD diagnosis in children at varying risk for ASD.

Methods: Participants were 64 children at high- or low-risk for ASD from diverse ethnic/racial backgrounds. High-risk children had at least one older sibling with ASD, while low-risk children had no known family history of ASD. Smiling behaviors were measured at 6 months of age during the Face-to-Face/Still Face paradigm. We focused on the Face-to-Face (parent interacts with infant normally for 3 minutes) and Reunion (parent re-initiates interaction with infant for 3 minutes after period of non-responsiveness) episodes. Parent and infant smiling was reliably coded for presence or absence on a frame-by-frame basis. Two smiling variables were calculated across episodes: Frequency of Smile Onsets and Contingent Responsive Smiling (smiles occurring within 1-second of partner's smile, controlling for overall level of infant and parent smiling). ASD diagnosis occurred at 36 months based on results from gold-standard autism diagnostic measures and clinical judgment. Children were divided into three groups: Low-Risk ($n$=24), High-Risk/No ASD ($n$=31), and ASD ($n$=9).

Results: Diagnostic group differences in parent and infant smiling variables were assessed by conducting a series of one-way ANOVAs. There were no diagnostic group differences in either of the parent smiling variables, suggesting that parents of high- and low-risk children smile at comparable levels and are similarly responsive during interactions with their infants. There were, however, differences between diagnosis groups in infant smiling behaviors. While there was no difference in the overall frequency of infant smiling, there was a group difference in contingent responsive smiling, $F(2,61)=3.58$, $p=.03$. Post hoc analyses revealed a significant difference between the High-Risk/No ASD ($M=.08$, $SD=.08$) and Low-Risk ($M=.13$, $SD=.08$) groups, $p=.04$. The ASD group did not significantly differ from either group.

Conclusions: This is one of the first studies to utilize a micro-coding approach to examine infant responsive social smiling in relation to autism risk. Interestingly, the overall level of infant smiling did not differ by infant risk group or eventual diagnosis; rather, responding to another's smile within a 1-second window differentiated the infants with a family history of ASD from typically developing controls. Infants eventually diagnosed with ASD did not differ from unaffected children on either smiling variable. Although it is difficult to interpret these results given the small number of diagnosed children in our sample, this suggests that responsive social smiling may represent an endophenotype related to genetic risk for ASD, rather than a specific risk factor for the disorder.

**156.045 45** Pragmatic Language Difficulties and Associations with Behavior Problems in Non-ASD Siblings of Children with ASD. M. Miller*[1], G. S. S. Young[1], T. Hutman[2], S. Johnson[2], A. J. Schwichtenberg[3] and S. Ozonoff[4], (1)*UC Davis MIND Institute*, (2)*University of California Los Angeles*, (3)*Purdue University*, (4)*University of California Davis Medical Center*

Background: In addition to being at heightened risk of developing ASD, siblings of children with ASD are at risk for other developmental concerns including structural language impairments (Drumm & Brian, 2013) and behavior difficulties (Schwichtenberg et al., 2013). However, pragmatic language has been underexplored in younger siblings of children with ASD. Low pragmatic competence has been linked to behavior problems (Ketelaars et al., 2010); whether such associations are amplified in very young children with a family history of ASD is unknown.

Objectives: Aims included (1) evaluating pragmatic language outcomes (both severity and categorical classification) at 36-months in non-ASD siblings of children with ASD, and (2) examining concurrent associations between pragmatic language and behavior problems.

Methods: Pragmatic language (measured by the Language Use Inventory, LUI) and behavior problems (using the Child Behavior Checklist, CBCL) were examined at 36-months in non-ASD siblings of children with ASD (high-risk, $n$=188) or typical development (low-risk, $n$=119). Risk group differences in pragmatic language were evaluated using ANCOVA (covariates: gender, structural language). Pragmatic impairment was defined as LUI scores $<10^{th}$ percentile; group differences in rates of impairment were evaluated using chi-square. Multiple hierarchical regression was used to evaluate concurrent associations between LUI

and CBCL scores controlling for risk group, gender, and structural language; moderation by risk group was examined.

Results: The high-risk group evidenced lower LUI scores than the low-risk group, $F(1, 303) = 21.99$, $p < .001$ and had higher rates of categorically-defined pragmatic language impairment (35% vs. 10%, respectively), $\chi^2 = 23.26$, $p < .001$. For the 65 high-risk participants classified as pragmatically impaired, 54% had atypical CBE outcomes: $n = 16$ broader autism phenotype (BAP), 10 speech-language problem, 6 behavior problem, and 3 global developmental delay. Of the 12 low-risk participants identified as impaired pragmatically, 3 received atypical CBE outcomes (all BAP).

Regression analyses revealed that LUI scores were significantly negatively associated with externalizing and internalizing behavior (that is, better pragmatic language was associated with fewer behavior problems). Risk group moderated the association between LUI scores and externalizing behavior ($p < .001$) with examination of simple slopes indicating that the significant association was limited to the high-risk group. Risk group did not moderate the LUI-internalizing behavior association.

Conclusions: Young children with a family history of ASD showed evidence of pragmatic language difficulties as early as 36-months, and pragmatic deficits were associated with externalizing and internalizing behavior problems. In the context of genetic risk for ASD, pragmatic language was associated with externalizing problems, but not in the absence of such risk. One possible mechanism underlying this stronger association in the high-risk group pertains to similar shared risk for both types of difficulties (Mulligan et al., 2009; Rommelse et al., 2011); indirect associations with shared risks may simultaneously put children with a family history of ASD at greater risk for both pragmatic language and externalizing problems. Follow-up of such samples will allow for clarification of likely bidirectional associations between pragmatic language and behavior problems. Close monitoring of pragmatic language development in this population may be warranted.

**156.047 47** Results of Two Screening Tools Impact Diagnostic Outcome. M. Khowaja* and D. L. Robins, *Georgia State University*

Background: In order for early autism intervention to help improve prognosis, early detection is crucial. A variety of screening tools exist; however, no screening tool can identify all children with ASD. In this study, the Modified Checklist for Autism in Toddlers (M-CHAT(-R)) was administered to parents of toddlers, and the Screening Tool for Autism in Two-Year-Olds (STAT) was administered to a subset of screen negative and screen positive cases.

Objectives: Examine whether diagnostic outcomes differ based on which measures children screened positive; in other words, does ASD-risk conveyed by M-CHAT(-R) and/or STAT relate to outcome?

Methods: Parents consented and completed the M-CHAT(-R) at their child's 18- and/or 24-month pediatric check-up; screen positive cases were contacted by researchers to complete the M-CHAT(-R) Follow-Up; those who continued to screen positive were offered a free diagnostic evaluation, including the STAT. Additionally, a subset of those who did not show risk on the M-CHAT(-R) completed the STAT, as well as a subsequent free evaluation if they demonstrated ASD risk on the STAT. The current sample (n=75; mean age at evaluation = 27.6 months, $SD = 2.8$) includes three sex- and age-matched groups: screen positive on both M-CHAT(-R) and STAT (BOTHpos), screen positive on M-CHAT(-R) and screen negative on STAT (M-CHATpos), and screen negative on M-CHAT(-R) and screen positive on STAT (STATpos). ASD diagnosis was based on ADOS(-2), structured parent interview, and clinical judgment.

Results: The sample was 64% male; race was 52% Black and 40% White. Chi-Square indicated that group (based on screening results) was related to diagnostic outcome, $\chi^2(2, 75)=8.50$, $p=.014$, Cramer's $V = .337$. Specifically, adjusted residuals (all $> \pm 1.96$) indicated that the STATpos group was less likely to have ASD (PPV = .32), and the BOTHpos group was more likely to have ASD (PPV = .72). Additionally, ADOS comparison scores were examined across screening groups as a more dimensional approach to understanding ASD symptomatology. Results revealed that screening group was significantly related to ADOS comparison score, $H(2) = 13.63$, $p = .001$. Post-hoc Mann-Whitney $U$ tests with Bonferroni corrections indicated higher ADOS

severity score in the BOTHpos group compared to the STATpos group, $U = 123.0$, $p < .001$. The M-CHATpos group was not significantly different from the other two groups on diagnostic classification or ADOS outcome. When groups were restricted only to cases diagnosed with ASD, the ADOS severity score did not significantly differ, $U = 2.50$, $p = .286$.

Conclusions: The BOTHpos group was more likely to be diagnosed with ASD and have higher ADOS severity than the STATpos group. However, across groups children with ASD did not differ in severity of symptoms. The current study used the STAT as both a level two screening measure for use among at-risk samples as it was originally intended, and as a tool to identify missed ASD cases. The results suggest that the highest likelihood of an ASD diagnosis is when a child screens positive on both screeners.

**156.048 48** Sex Differences in Parent Report of Adaptive Behavior of Children at Risk for Autism Based on the Modified Checklist for Autism in Toddlers (M-CHAT). N. N. Ludwig*[1], D. Robins[1], L. B. Adamson[1] and D. A. Fein[2], (1)*Georgia State University*, (2)*University of Connecticut*

Background: The Positive Predictive Value (PPV) of the Modified Checklist for Autism in Toddlers (M-CHAT), a parent report early screening tool, is higher for males than for females (Ludwig et al., IMFAR 2011), and parents endorse different items on the M-CHAT based on sex (Ludwig et al., 2012). However, sex differences have not emerged on direct measures of ASD symptoms and cognitive skills in children who screen positive on this screening tool (Ludwig et al., IMFAR 2013).

Objectives: The current study examined sex differences in parent report of adaptive behavior in toddlers who received an ASD evaluation based on M-CHAT screen positive status in order to explore how parent report may contribute to the differential PPV of the M-CHAT in boys and girls.

Methods: The sample included 250 males and 106 females (mean age=25.3 months, *SD*=4.55) who were evaluated based on screen positive (at risk) status on the M-CHAT, a parent questionnaire administered at pediatric well-visits. Evaluations included autism diagnostic measures (ADOS, ADI-R, CARS), cognitive testing (Mullen Scales of Early Learning; MSEL), as well as parent report of history and adaptive behavior (Vineland Adaptive Behavior Scales; VABS). One hundred seventy-six toddlers were diagnosed with ASD at the time of evaluation (139 males, 37 females) and 180 toddlers were not (111 males, 69 females); 71% of toddlers not diagnosed with ASD were diagnosed with another developmental delay.

Results: Four ANOVAs were conducted with sex and ASD status (ASD vs. non-ASD) as fixed factors and the VABS domain scores as dependent factors. There was no interaction or main effect of sex for the Daily Living Skills or Socialization domain scores; however toddlers diagnosed with ASD demonstrated weaker skills in these areas ($p$'s<.05). Although children diagnosed with ASD also demonstrated weaker parent reported Communication and Motor Skills than toddlers without ASD, there was a significant interaction between sex and ASD status such that girls diagnosed with ASD were rated lower on these domains than boys diagnosed with ASD ($p$'s<.05).

Conclusions: This pattern of findings suggests that there are differences in parent report of adaptive skills in boys and girls considered at risk for ASD based on the M-CHAT. Generally, toddlers with ASD demonstrated weaker parent-reported adaptive behavior than toddlers without ASD, but girls with ASD were rated lower on Communication and Motor Skills than boys with ASD. These findings are in contrast to recent findings that demonstrated no sex differences on direct measures of language and communication (MSEL) in the same sample (Ludwig et al., IMFAR 2013). These findings may suggest that parents of girls with ASD may under-report their child's everyday adaptive skills, or that our current direct observation measures may not capture the full range of behavioral sex differences in children with ASD. In addition, these data also suggest that parent perception of child behavior may differ based on sex, which could influence the way in which parents fill out the M-CHAT.

**156.049 49** Stability of Autism Diagnosis in Children Under 24 Months. L. H. Shulman*, K. F. Hottinger, M. D. Valicenti-McDermott, R. M. Seijo, D. J. Meringolo, N. L. Tarshis, E. D'Agostino and S. D. Rabbanifar, *Albert Einstein College of Medicine*

Background: The early diagnosis of autism spectrum disorder (ASD) has become an important clinical and public health goal. While it has been well established that an ASD diagnosis

made between 2 and 3 years of age is stable, less is known of the stability of an ASD diagnosis in younger toddlers.

Objectives: To prospectively examine the stability of an ASD diagnosis made by age 24 months (mo) and to examine initial clinical and demographic factors associated with retention of the diagnosis.

Methods: 108 children were diagnosed with ASD by age 24 mo at a University-affiliated inner-city diagnostic Early Intervention program between 1998 and 2009. Diagnoses were made by a multidisciplinary team (developmental pediatrics, psychology, speech and language pathology), based on the DSM-IV Pervasive Developmental Disorder criteria, Childhood Autism Rating Scale (CARS), and, in some, the Autism Diagnostic Observation Schedule (ADOS). At least one year after initial diagnosis, families were invited to return for updated developmental evaluation and ADOS to confirm ASD diagnosis. Data collected included initial assessment (demographics, cognitive level, and autistic features) and follow up information (interventions received and current educational placement). Statistical analysis included chi-square, t-test and nonparametrics.

Results: The mean age at initial diagnosis was 20±3mo (range:12-24mo),75% male, mean initial CARS score of 35±4, developmental quotient <70 in 57%. Autism was diagnosed in 25% (27/108) and ASD/Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) in 75% (81/108). Of the 108 children, 77 returned for follow up developmental evaluation at least one year after initial diagnosis. There were no differences in age at diagnosis, ASD severity, or demographic characteristics between those who returned for follow up (N=77) and those who did not (N=31). The mean age of the children who returned for follow up was 54.4±29.9mo. All 22 of the children initially diagnosed with autism and 82% (45/55) of those diagnosed with ASD/PDD-NOS continued to meet criteria for ASD based on ADOS (available in 40/77), CARS, and/or autism-specific school placement. Ten children did not meet criteria for Autism or ASD at follow up. These children had significantly lower initial CARS scores (32.2 ±1.4 vs. 35.3 ± 4.8, p< 0.001) and were less likely to have presented with mannerisms at initial diagnosis (60% vs. 91%; p=0.006), without significant differences in demographics, cognition, length of time between initial diagnosis and follow up, or types of intervention as compared to those who retained an ASD diagnosis. Specifically, children who continued to meet criteria for ASD at follow up were more likely to have presented with motor mannerisms (77.6% vs. 20%; p<0.001) before age 24mo.

Conclusions: In this sample, an ASD diagnosis made by experienced clinicians in toddlers 12 to 24mo of age was quite stable. The diagnosis of Autism was more stable than PDD-NOS. The presence of motor mannerisms at initial diagnosis was associated with retention of ASD diagnosis at follow-up.

**156.050 50** The Impact of Intervention on Parent-Child Communication Following Early ASD Screening. K. Suma*, L. B. Adamson, R. Bakeman and D. L. Robins, *Georgia State University*

Background: A major component in the argument for early ASD screening is that it may hasten a child's enrollment in early interventions, which studies show can be critical in facilitating development. However, there is only limited information about how obtaining a diagnosis leads parents to seek interventions in the period just after diagnosis and how these early increases in intervention might affect parent-child interactions and parent perception of child communication.

Objectives: The current study sought to explore how early diagnosis affects enrollment in interventions and, in turn, how interventions that occur soon after diagnosis affect parent-child interactions and parent perception of child communication. We hypothesized that increases in intervention will be evident in parents' contributions to interactions with their child and increased perception of their success in supporting their child's communication.

Methods: 66 toddlers who screened positive on the M-CHAT with Follow-Up (a 2-stage screening tool for ASD) were observed just before a diagnostic evaluation (T1; mean age = 23.8 months) and approximately 7 months after diagnosis (T2); 39 were diagnosed with ASD and 27 with a non-ASD developmental delay (DD). At each visit, 30-minute semi-naturalistic observations of parent-child interaction were video recorded and subsequently reliably rated for child's supported joint engagement, coordinated joint engagement, parent scaffolding, topic

sustainability, and fluency and connectedness of topic. Parents completed a questionnaire about the child's communication (Parent Perception of Language Development; PPOLD) that generates two factor scores, parent success (how effective the parent thinks he or she is in supporting communication) and child difficulty (parent's perception of the child's difficulties communicating). Parents also reported the type and number of hours of child intervention. Children were divided into two groups based on whether they experienced an increase in intervention between T1 and T2; 35% (*n* = 23, 18 with ASD) were assigned to the increased intervention group because of an increase in hours and/or specificity of the intervention.

Results: Mixed design ANOVAs with intervention group (no increase, increase) as the between-subjects factor and time as the within-subjects factor indicated significant increases over time in the 5 ratings of parent-child interaction and in parent success, but not in child difficulty (partial eta-squares > .20, *p*s < .001 for all). Increases in parent scaffolding and topic sustainability were greater and increases in supported joint engagement, fluency and connectedness, and parent success were marginally greater in the increased intervention than in the no increased intervention group (group by time interaction *p*s = .02, .01, .08, .10, and .07, respectively).

Conclusions: This study demonstrates that relatively small increases in intervention that follow early diagnosis can have a marked impact on parent-child interactions and parents' beliefs about their ability to help their children communicate. These findings underscore the importance of increasing intervention as soon as possible after diagnosis and highlight the critical need for understanding how to help parents rapidly arrange appropriate early intervention.

## 157 Genetics

**157.051 51** Aberrant Genome-Wide DNA Methylation Identified in Disorders Associated with 7q11.23 Copy Number Variation. E. Strong*[1], D. Butcher[2], C. B. Mervis[3], C. A. Morris[4], R. Weksberg[2] and L. R. Osborne[1], (1)*University of Toronto*, (2)*The Hospital for SickKids*, (3)*University of Louisville*, (4)*University of Nevada School of Medicine*

Background: Autism spectrum disorders (ASD) arise from many different genetic alterations. By understanding all forms of ASD we will be able to piece together a picture of key, common changes that occur in the developing brain, as well as those that are unique and lead to specific phenotypic features. The complex neurodevelopmental disorders that arise from either deletion (Williams syndrome, WS) or duplication (7q11.23 duplication syndrome, Dup7) of 26 genes on chromosome 7q11.23 result in phenotypic spectra that include both core and associated features of ASD and so provide a unique window into genes and pathways that contribute to symptoms. Dup7 has recently been identified as an ASD-associated CNV, with four *de novo* cases identified during screening of a large autism cohort, and features common to ASD, such as speech disorder and repetitive behaviors, have been reported in other individuals with Dup7. We, and others, have reported socio-communicative difficulties in children with WS that overlap significantly with ASD and >20% of children with WS are classified as "ASD" on the ADOS-2.

Objectives: Since five genes within 7q11.23 have been implicated in epigenetic regulation, we hypothesized that deletion or duplication of this region would disrupt the epigenetic profile of individuals with WS or Dup7, and that this disruption could play an integral role in the ASD phenotypes. Our objective was to investigate epigenetic regulation, specifically DNA methylation, in these disorders.

Methods: We measured genome-wide DNA methylation in whole blood from 20 children with WS, 10 with Dup7 and 15 age- and sex-matched typically developing controls, using the Infinium HumanMethylation450 array from Illumina. Differential methylation was assessed using a stringent cut off of 17% gain or loss of methylation (adjusted $p \leq 0.05$). The functional impact was assessed using real time PCR of differentially methylated (DM) genes from whole blood RNA.

Results: We identified over 1,000 DM probes across the WS and Dup7 cohorts that correspond to approximately 500 unique genes. Many of the DM probes span genes involved in neurodevelopment. Hierarchical clustering of the methylation profiles of participants with WS or Dup7 correctly grouped each individual with his/her respective syndrome, and distinct from controls, suggesting the methylation differences may contribute to the phenotypic differences between these disorders. Moreover, of the 46 DM

probes that overlapped between WS and Dup7, the majority showed opposite levels of methylation, suggesting a dose-dependent change in DNA methylation at these sites. For the few DM genes that were expressed in blood we showed corresponding changes in expression level.

Conclusions: We have identified aberrant genome-wide DNA methylation in these deletion and reciprocal duplication syndromes with features of ASD. This study identified striking differences in methylation profiles, with corresponding changes in gene expression, suggesting that epigenetic pathways may be involved in pathogenesis and confirming that one or more genes within 7q11.23 is important for proper DNA methylation at specific sites. Future studies will involve correlative epigenotype-phenotype analyses to understand the impact of dysregulated genes and pathways on ASD features in children with WS or Dup7.

**157.052 52** Whole Exome Sequencing of ASD in Korean Population. H. J. Yoo*[1], S. A. Kim[2], J. Kim[3], J. E. Park[1], M. Park[2] and N. Kim[3], (1)*Seoul National University Bundang Hospital*, (2)*Eulji University Medical College*, (3)*Korea Research Institute of Bioscience and Biotechnology*

Background: Whole exome sequencing (WES) techniques provide the opportunity for elucidation of the genetic causes of ASDs.

Objectives: The objective of this pilot study is to examine genetic variant of ASD using WES in family samples from Korean population and developing analytic pipeline for further studies with larger samples.

Methods: For ascertainment of subjects, we used Korean versions of Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2008) and Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 1994) along with Social Communication Questionnaire (SCQ) (Rutter et al.,2003) and Social Responsiveness Scale (SRS) (Constantino, 2005). We identified 13 families with ASD, composed of probands, biological parents and unaffected siblings, from pooled database of Korean Autism Genetic Study Consortium. We selected severe, typical subjects of ASD for attaining relative homogeneity of the phenotype, with criteria of; 1) probands meeting full criteria of autistic disorder of DSM-IV-TR, 2) age between 48~156 months, 3) nonverbal or phrase speech level of language development, and 4) scores of lifetime algorithms of ADI-R and SRS are within 25 percentile of the database.

We had performed whole-exome sequencing for 13 probands, minimum 50X on target. At least 94% of target area were covered more than 5 sequence reads. In order to find de novo mutation candidates, we had performed additional high-coverage whole-exome sequencing on two pooled samples from mothers (250 million paired-end reads) and fathers (236 million paired-end reads) of probands. All the sequence reads were mapped onto the human reference genome (hg19 without Y chromosome). Variant discovery had been done by BWA, Picard, GATK, and in-house custom annotation pipeline. We had selected de novo mutation candidates (nonsynonymous, splice site, and coding indel mutation) from each proband which are not detected in two pooled samples and not reported in dbSNP137 and in-house Korean databases.

Results: We had selected 29 de novo mutation candidates from 21 genes; *ABCF3, ADRB1, AKNA, AKT1S1, CELSR3, CHKA, FOXK2, IFI27L2, ITFG3, KCTD9, KDM6B, LOXL2, MYH14, PAX2, POLRMT, RBM20, SLC47A2, SOX7, TCTE1, TXNDC11*, and *USP8*. In order to validate candidate variants, we performed Sanger sequencing. As the results, we could confirm 5 de novo missense mutations from 5 different genes including; *AKNA (*AT-hook transcription factor*), CELSR3 (*cadherin, EGF LAG seven-pass G-type receptor 3*), KCTD9 (*potassium channel tetramerization domain containing 9*), MYH14* (myosin, heavy chain 14, non-muscle) and *TCTE1 (*t-complex-associated-testis-expressed 1). There was no de novo mutation shared in more than two probands.

Conclusions: In the WES of family samples of ASD, we observed 5 de novo missense mutations from 5 different genes, including *AKNA, CELSR3, KCTD9, MYH14* and *TCTE1*. None of the mutations reported as possible causative genetic mutation in ASD in the previous reports. Of those, *CELSR3* is known as playing an important role in planar cell polarity and brain development and maintenance, as well as hippocampal maturation and connectivity (Boutin et al., 2012; Feng et al., 2012). *MYH14* has been reported as related with hearing loss, cleft lip and myopathy in human subjects (Choi et al., 2011, Yang et al., 2005).

**157.053 53** CD38 Gene Polymorphism on Eye-Gaze Ability in Human Social Interaction. I. Lee*[1], T. Lehtimaki[2], K. Puura[2] and D. H.

Skuse[1], (1)*UCL Institute of Child Health*, (2)*Tampere University and University Hospital*

Background: Eye contact provides important social and emotional information in human communication. The direction of an individual's eye-gaze may indicate to others where his or her attention lies. In autism, this ability is impaired. Social interaction abilities such as eye-gaze communication are heritable and are possibly due to genetic variations. CD38 has been reported to be critical for social processing and behaviour by regulating oxytocin secretion. We hypothesised that CD38 gene polymorphisms could contribute to individual variability in the accuracy of detection of another's direction of gaze.

Objectives: We tested our hypothesis by examining the association between CD38 gene polymorphisms and a standardized measure of direction of gaze detection, in both children with autism and their family members. Our previous work had standardized the measurement of eye-gaze communication impairment in typical population controls, for both age and sex. We could therefore measure individual differences in accuracy on this task in standard deviation scores, using the same instrument for all subjects.

Methods: 757 participants from 209 families were recruited, including 215 children with clinically diagnosed autism (98.4% Caucasians; mean age=11.3±3.4 years; Full Scale IQ=97.4±18.1; male/female ratio=4.4:1), their parents (mean age=42.9±6.0 years; Full Scale IQ=112.6 ±12.6) and their siblings (mean age=12.1±5.1 years; Full Scale IQ=105.6±20.1). All family members completed the standardized social cognition tests, including the test of Eye-Gaze Detection Accuracy. Autistic traits were measured using the Developmental, Dimensional and Diagnostic Interview (3Di) and the Autism Diagnostic Observation Schedule (ADOS).

Biological samples were collected for DNA extraction. Seven CD38 SNPs were identified for analysis, based on previous reports of an association with social skills in ASD. SNP genotyping was done using Kaspar assays. Genetic associations between genotypes and task were analysed using PLINK. Bonferroni corrections were applied for multiple SNPs and phenotype testing. Transcription factor Affinity Prediction (TRAP) was performed to predict regulatory transcription factor binding at intronic SNPs.

Results: We found that CD38 SNP rs3796867 was significantly associated with the eye-gaze endophenotype (p=0.019; p=0.00014 after Bonferroni correction). The task z-scores (mean ± standard error) were strongly related to genotype: AA [-1.14±0.56]; AG [-0.61±0.13]; GG [-0.33±0.064]. The mean z-score of those with A-allele was -0.60±0.1 compared with those with G-allele only -0.33±0.06 (paired t-test, $p<1x10^{-4}$) compiled across family members.

Conclusions: Eye-gaze direction detection was significantly impaired in the participants with the ancestral A-allele of rs3796867. This is an intronic SNP located between CD38 gene exons 1 and 2. TRAP predicted some important transcription factors such as PAX2, FOXD3, FOXA1, HFH8 (FOXf1), ZNF333 and SRY could have differential binding affinities to the G and A alleles of the SNP. Accordingly, the regulation of CD38 gene expression could influence individual differences in ability to detect the direction of another's eye gaze, hence potentially influencing competence in human social interaction.

**157.054 54** Game of Exomes: Battle of the Rare Variants for Association with Autism Spectrum Disorder. N. D. Dueker*[1], A. J. Griswold[1], H. N. Cukier[1], E. R. Martin[2], S. H. Slifer[2], J. Jaworski[2], I. Konidari[2], P. L. Whitehead[2], M. A. Schmidt[2], J. R. Gilbert[2], M. L. Cuccaro[2], J. L. Haines[3] and M. A. Pericak-Vance[2], (1)*University of Miami*, (2)*University of Miami Miller School of Medicine*, (3)*Case Western Reserve University*

Background: Autism spectrum disorder (ASD) is a highly prevalent developmental disorder, affecting an estimated 1 in 88 individuals, and is associated with significant morbidity. Despite demonstrating high heritability estimates, only a small proportion of the genetic risk for ASD is explained. While previous research, including genome wide association studies, has focused on the effects of common variants, recent exome sequencing studies suggest that rare variants (RVs) contribute significantly to ASD risk.

Objectives: To identify RVs associated with ASD using two approaches; 1. An agnostic approach testing all genes on the Exome Array for association with ASD 2. A candidate gene approach testing ~1,000 genes previously implicated in ASD for association with ASD, including 254 genes previously reported as associated with ASD in a gene-based analysis using whole exome sequencing data.

Methods: Participants were drawn from a large, family-based study of ASD and included 995 unrelated cases and 650 controls that were genotyped using the Illumina HumanExome-12v1 Array. To identify genes associated with ASD we performed gene-based analyses testing autosomal genes genotyped on the Exome Array for association with ASD. The sequence kernel association optimal test (SKAT-O) was used for these analyses. All analyses were performed within our genetically-defined White, Non-Hispanic sample. A Bonferroni correction was made to adjust our alpha levels of significance.

Results: We tested a total of 12,922 genes across the genome for association with ASD in our sample. While no genes were statistically significant, 14 genes were nominally associated with ASD ($p<0.001$). Of the ~1,000 ASD candidate genes tested, 19 were nominally associated with ASD ($p<0.01$), with the most significantly associated being adenylate cyclase 5 (*ADCY5*) (SKAT-O p=0.002) and dynein, axonemal, heavy chain 5 (*DNAH5*) (SKAT-O p=0.001).

Conclusions: While our study failed to identify RVs to be significantly associated with ASD, we did identify several nominally significant associations providing suggestive evidence for a role of RVs in ASD risk. These suggestive associations include A*DCY5* which is an excellent ASD candidate as it plays an important role in G-protein signaling and two separate reports have identified cases with *de novo* mutations in the gene. Further investigation into the role of RVs in ASD with larger sample sizes is necessary.

**157.055 55** Genome-Wide Gene-Environment Analysis Identifies Genetic Variation within A2BP1 As a Potential Modifier of the Risk Effect of Maternal Smoking on the Expression of Autistic Traits in Middle Childhood. D. Rai[1], D. H. Skuse[2], W. Mandy[2], J. Golding[1], D. M. Evans[1], N. J. Timpson[1], J. P. Kemp[1], W. L. McArdle[1], S. M. Ring[1], G. Davey Smith[1] and B. St. Pourcain*[1], (1)*University of Bristol*, (2)*UCL Institute of Child Health*

**Background:** Maternal smoking during pregnancy has been discussed as a potential risk factor for the increase of autistic symptoms in children, though findings have been inconsistent. It is possible however that maternal smoking might only elevate the expression of autistic symptoms in genetically susceptible individuals, and thus GxE may conceal the true underlying relationship between risk factor and behavioural outcome.

**Objectives:** We aimed to identify genetic moderators of the risk effect of maternal smoking on the expression of autism-related social communication difficulties during childhood and adolescence using a genome-wide GxE analysis.

**Methods:** We performed a 2-stage genome-wide GxE analysis with respect to social communication problems as captured by the Social and Communication Disorders Checklist (SCDC). Measurements were assessed in a large UK population-based birth cohort at 8, 11, 14 and 17 years of age (Avon Longitudinal Study of Parents and Children, $N \leq 5539$). During the first stage, we performed a genome-wide screen for differences in phenotypic variance per genotype (Levene's test) using 2.5 million imputed or genotyped SNPs and investigating each time-point individually. This identified a set of variants, which is likely to be involved in interactions. During the second-stage, we investigated all independent signals with respect to maternal smoking during the first trimester (adjusted for child's age and sex), performing a joint likelihood ratio test for both G+GxE and E+GxE respectively using negative binomial regression.

**Results**: Maternal smoking during the first trimester was identified as a strong predictor of increased autistic traits at 8 years of age ($\beta=0.23(0.05)$, measured in log-counts of social-communication problems, $P=4.4\times10^{-7}$), but the risk effect declined during the course of development. During stage one of our GxE screen, we identified 132 independent offspring SNPs (Levene-$P<10^{-5}$, LD based clumping: $r^2=0.2$, ±500kb, in addition to all SNPs in known ASD candidate regions with $P<10^{-4}$) across all 4 time-points, which are likely to be involved in interaction effects. The strongest E+GxE signal (Levene-$P=5.2\times10^{-5}$, $P_{GxE}=0.00016$ ($P_{GxE\_adj}=0.021$), $P_{E+GxE}=1.7\times10^{-9}$) was observed for variation in the ASD-candidate gene *A2BP1* (alias *RBFOX1*) and was associated with social-communication problems at 8 years of age. There was no evidence for a genetic main effect ($P_G=0.96$). Stratification by genotype, showed that the risk effect of maternal smoking was only present in homozygote carriers of the major (risk) allele (0 risk allele: $\beta$(smoking) = -0.23(0.20), P =0.27, 1 risk allele: $\beta$(smoking) = 0.057(0.084),

P=0.50, 2 risk alleles: β(smoking)=0.35(0.057), $P=5.8x10^{-10}$). The interaction was attenuated with progressive age due to the decline in risk effect of smoking. We found no joint G+GxE effect ($P<10^{-5}$), which provided more evidence for association than G alone. Replication of the interaction signal is currently being sought within independent cohorts.

**Conclusions:** Our variance-based genome-wide screen identified a small set of SNPs that are probably involved in interactions either with environmental or other SNP variation. We identified one GxE interaction effect, which, if replicated, might indicate that offspring of some smoking mothers are at particularly high risk for social-communication problems in childhood and adolescence.

**157.056 56** High Transposable Element Content in Strong-Association Autism-Risk Genes. E. L. Williams*, M. F. Casanova and A. E. Switala, *University of Louisville*

Background: Rates of mutation vary by gene, reflective of different trends in overall stability. These variations in stability are due to a number of factors, one of which relates to overall transposable element (TE) content within the gene.

Objectives: We have elected to study rates of TE content across high-risk autism-related genes as compared to randomized controls in order to gauge one aspect of genetic instability in these genes.

Methods: Our autism data were collected using the *AutismKB* database, while matched numers of controls were generated using a random gene generator. The database, *TranspoGene*, provided listings of TE content for our study. Due to the nature of our distributions, a nonparametric Kuiper test was utilized as well as logistic regression.

Results: We found that autism genes housed significantly greater TE content than randomized controls and that for every doubling of TE content, a given gene was 17% more likely to be associated with our autism group.

Conclusions: Our results suggest that autism genes may share a relative instability in relation to their TE content, leading to more frequent mutations. While many studies have attempted to address functional commonalities amongst autism-related genes, ours is the first study which seeks commonality at the level of the gene rather than its gene product. In understanding how and when such mutations may arise, we may better understand what roles they play in autism's etiology.

**157.057 57** Increased Risk of Autism Spectrum Disorders in Boys with XYY. J. Ross*[1], D. Roeltgen[2], N. Tartaglia[3], B. M. Winder-Patel[4] and J. Miller[5], (1)*Thomas Jefferson University*, (2)*University of Pennsylvania*, (3)*University of Colorado*, (4)*The Children's Hospital of Philadelphia*, (5)*Center for Autism Research, The Children's Hospital of Philadelphia*

Background:

A known, highly penetrant genetic risk factor for Autism Spectrum Disorders (ASD) is the presence of a second Y chromosome, as found in the male sex chromosome aneuploidy disorder, 47,XYY syndrome (XYY). XYY occurs in ~0.1% of population-based males but is reported in 1% of males with ASD. Approximately 19 to 36% of males with XYY are reported to satisfy ASD diagnostic criteria.

Objectives: Characterize the autism phenotype in boys with XYY and evaluate the impact of prenatal versus postnatal ascertainment on the phenotype.

Methods: We performed a detailed ASD evaluation in 36 boys with karyotype-confirmed XYY (mean age 9.7±3.1 y [range 4-16 y]) using the Social Communications Questionnaire (SCQ, all 36 subjects), the Social Responsiveness Scale (SRS, 29 subjects), the Autism Diagnostic Interview-Revised (ADI-R, 29 subjects), and the Autism Diagnostic Observation Scale (ADOS**,** 15 subjects). Verbal abilities were evaluated with the Differential Ability Scales (DAS, all 36 subjects). We also evaluated possible ASD modulating factors including age, verbal abilities, socioeconomic status (SES), and timing of XYY diagnosis (prenatal versus postnatal).

Results: Diagnosis of XYY was made prenatally in 17 (47%) boys and in childhood (for developmental/ behavioral issues) in 19 (53%) boys. Intellectual functioning was, on average, within the normal range (mean DAS General Conceptual Ability standard score 92±14). A total of 91% had received speech and/or reading therapy, and 91% received occupational and/or physical therapy. Sixteen of 36 (44%) scored

above the SCQ cutoff score for screening for ASD. Fourteen of 29 (48%) had scores in the clinical range (>mean+2.6 SD) on the SRS autistic behavior subscale. Of 29 boys with XYY, 9 (31%) met ADI-R ASD criteria, indicating a much higher rate of probable ASD than that of the general population. Seven of 15 (47%) boys with XYY met ADOS ASD criteria and 4 of these 7 also met Autism criteria. Age, SES, and verbal DAS scores were not correlated with SCQ, ADI-R, or SRS scores. ASD metrics were more severe in the postnatally ascertained boys, but there was a significantly increased ASD risk in both XYY cohorts. The proportion of boys meeting ASD criteria on the ADOS was similar in the prenatally versus postnatally diagnosed cohorts (43% vs. 50%).

Conclusions: These data strongly support the group-wide findings of increased ASD risk in XYY, and indicate that the prevalence of ASD in prenatally diagnosed XYY is similar to that in fragile X syndrome, the most common known genetic cause of autism. XYY represents a relatively well-defined genetic ASD model, compared to idiopathic ASD, which is more heterogeneous with regard to etiological/risk factors and pathogenesis. The strong likelihood that increased Y-chromosome dosage and increased risk of ASD are significantly associated deserves further investigation and may identify a genetic component of the marked male predominance in ASD.

**157.058 58** Integration of Copy Number and Exome Sequence Data in a Queryable Database for the Investigation of ASDs. E. McArthur*[1], X. Zhang[1], E. R. Gamazon[1], J. S. Sutcliffe[2], E. H. Cook[3], L. K. Davis[1] and N. J. Cox[1], (1)*University of Chicago*, (2)*Vanderbilt University*, (3)*University of Illinois at Chicago*

Background: Although ASD has a significant genetic component, a heterogeneous etiology makes gene discovery complex. With the advent of efficient and affordable sequencing tools, genomic data is becoming widely available in public databases. Two data types of particular relevance for ASD investigation are copy number variants (CNVs) and whole exome sequence data. Exome sequence data has been previously shown to help identify causative genes and variations in complex disorders. *De novo*CNVs have been found in dosage-sensitive regions, which are typically stable in healthy controls. Because of the heterogeneity of ASD, it is necessary to integrate CNV and exome sequence data to help identify candidate genes.

Objectives: To develop a pilot queryable and scalable database for effective integration of whole exome sequence data and CNV data in order to identify additional genes and variants of interest in ASD.

Methods: A pilot database was developed using available data for 24 probands—23 male and 1 female. Exome sequence data were variant-called with GATK and TrioCaller, exported to a variant call format (VCF), and annotated with ANNOVAR. The VCF contained information such as position, phased genotype, raw read depth, and multiple measures of deleteriousness and conservation. CNV calls were generated by CNVision using Illumina 1M array data and contained information including position, copy number, ancestry, gender, and the calling algorithm used for detection (PennCNV, GNOSIS, and/or QuantiSNP). A MySQL database with four relational tables containing all variant and proband data was developed. The database was queried for rare hemizygous deleterious variants by specifying SNVs with a minor allele frequency less than 5% and possibly deleterious LJB_PolyPhen2 scores which are within areas of CNV deletion.

Results: Eight rare hemizygous and putative deleterious SNVs were found in the population. Three of the eight (rs59056023, rs17844333, rs115218749) were found in CNV deletion regions within the gene *PCDHA9*, encoding protocadherin alpha 9. By issuing further queries, it was determined that nine of the 24 individuals (37.5%) have at least one region of deletion within the *PCDHA9* gene.

Conclusions: Through this investigation of rare, hemizygous deleterious variants in ASD probands, we present an efficient approach for effectively integrating different data types and demonstrate that the approach is simple, although robust with even a small sample of data. Database queries are easily customizable for multiple parameters, such as deleteriousness, copy number, conservation, exonic function, MAF, among others. Our initial application of the methodology suggests a further need for investigation into the characterization of rare SNVs within CNV regions. Further attention to *PCDHA9* is warranted, especially given its predicted role in establishing and maintaining

neuronal cell-cell connections. Other applications of this database framework and integration of additional types of genomic and phenotypic data for ASD investigation will be considered as future directions.

**157.059 59** Interactions Dynamics of 16p11.2 Genes Across the Developing Human Brain. G. N. Lin*[1], R. Corominas[1], X. Yang[2], D. E. Hill[3], M. Vidal[3] and L. M. Iakoucheva[1], (1)*University of California San Diego*, (2)*Dana-Farber Cancer Institute*, (3)*Harvard Medical School*

Background: Autism spectrum disorders (ASD) has a strong genetic component. Several Copy Number Variants (CNVs) have been firmly implicated in ASD. Recurrent CNV deletions and duplications of ~600 kb at chromosome 16p11.2 confer high susceptibility to ASD in up to 1% of ASD patients. Moreover, both *de novo*deletion and duplications of that CNV have been recurrently identified in ASD patients. Functional studies have shown that reciprocal deletion or duplication of 16p11.2 results in brain overgrowth or reduced brain volume in mice, respectively, further supported using zebra fish model. Recently, induced pluripotent stem cell technology is also starting to relate CNV deletions to cellular phenotypes in humans. Several binary protein-protein interactions (PPI) have already been mapped to 16p11.2 genes. However, the dynamic of interaction cold/hot spots of 16p11.2 genes throughput human brain development is still vastly unknown.

Objectives: We focused our study on the pattern of protein interactions and co-expression of the 33 proteins encoded by 16p11.2 CNV genes. We aimed to identify particular co-expression patterns of interacting protein pairs in order to determine subsets of interactions occurring at specific stages of brain development. We present a temporal-spatial assessment of 16p11.2 genes interactions throughout early human brain developments, from early development (8 post conception weeks) to young adult (40 yrs).

Methods: We used the spatio-temporal gene expression dataset from BrainSpan project, comprising various brain regions across different stages of brain development to identify the time-space interaction cold/hotspots within the PPI network. Tissue samples were divided into four anatomic regions: prefrontal cortex (FC), temporal and parietal regions (TP), sensory-motor regions (SM), and subcortical regions (SC); and five stages of brain development: early fetal, mid-late fetal, infancy to childhood, adolescence and young adult. It resulted in 20 different time-space categories. Spearman correlation coefficient was calculated for each gene pair in each category. Several rigorous controls have been chosen for the analysis (such as randomly selected genomic regions with the same number of genes and PPIs, common CNVs from the database of Genomic Variants or extracted from the 1000 Genomes dataset). The statistical significance of co-expression enrichment of PPIs in specific category when comparing to a control is calculated using Fisher's exact test.

Results: We first observed that interactions from 16p11.2 genes are distinctly clustered in three general temporal regions: fetal, childhood/adolescence, and young adult, based on their Spearrman correlations patterns. The separation of the interaction groups in 16p11.2 could indicate a different functional relevance of specific PPI subset in precise time and brain region. Furthermore, when comparing to the controls, in early fetal, the interacting pairs involving 16p11.2 protein products showed significantly depleted co-expression (coldspots), specifically at FC and TP regions. On the contrary, in adolescence, the interacting pairs showed significantly more co-expression (enrichments or hotspots), specifically at SM and TP regions. These patterns were not observed when the same analysis was not restricted to physical interacting pairs in 16p11.2.

Conclusions:

This analysis would provide valuable information about expression patterns of the shared and unique PPIs in different disorders detected by cross-disorder interactome mapping.

**157.060 60** Network Analysis of Protein Interaction Module of AutDB Database. U. Kuppuswamy[1], C. C. Swanwick[2], S. Muend*[1] and S. B. Basu[3], (1)*MindSpec Inc*, (2)*MindSpec Inc.*, (3)*MindSpec, Inc.*

**Background:** Hundreds of genetic variants have been linked to autism, complicating the understanding of disease etiology. One approach to decode this heterogeneous genetic landscape is to identify shared molecular pathways of autism candidate genes that are known to often work together in a common biological context. In order to systematically catalogue interactions among

autism genes, we have developed the protein interaction (PIN) module that integrates into our previously developed autism database (AutDB).

**Objectives:** The goal of this work is twofold: To (1) maintain a comprehensive, up-to-date integrated module (PIN) comprising of systematically curated, manually verified, molecular interactions of autism genes (2) perform network analysis of interactions among autism-linked genes using PIN module.

**Methods:** PIN module manual curation process entails data extraction from published, peer-reviewed literature. Post consultation with public databases (BioGRID, HPRD), PubMed searches are performed and three types of binding (protein, RNA, promoter) and three types of regulation (protein modification, direct regulation, autoregulation) interactions are manually extracted. Utilizing this data in PIN module, we built networks for a reference gene set consisting of rare and syndromic ASD genes. Next, we identified all instances of direct molecular interactions among the autism risk genes in this network. To evaluate the statistical significance of these direct interactions, we compared the topological properties of the network with 1000 randomly generated controls. Furthermore, based on the hypothesis that physically interacting proteins share common biological functions, we extracted all the "one-hop" genes linking two autism risk genes. The significance of the extracted "one-hop" genes was further evaluated by analyzing their spatial and temporal expression patterns in the developing brain.

**Results:**

The PIN dataset has grown rapidly since its first release in June 2011. As of September 2013, it includes 184 genes, 23214 interactions, and 1516 references. Our multi-faceted analysis of AutRef84 dataset containing rare and syndromic genes related to autism revealed small-world characteristics of ASD networks. Compared to 1000 controls of equal size (number of nodes and edges), the direct interactions network showed higher clustering coefficient (CC), lower average shortest path length (ASP) and lower diameter (D), indicating tight connectivity among the ASD risk genes. Among the numerous "one-hop" proteins extracted from the AutRef84 main interactome, a significant number of them overlapped with existing ASD candidate genes. Coexpression analysis using BrainSpan database indicated enriched connectivity among these candidates in brain region subsets at specific time periods, signifying their convergent role during development.

**Conclusions:** PIN module serves as an invaluable resource for several bioinformatic analyses. Starting with a small list of seed genes, our analysis resulted in several convergent candidate autism genes which further showed spatial and temporal specificity aligned to the specific gene expression patterns observed during development. The PIN module and network analysis of similar nature would serve as a framework to guide further autism research and enable identification of diagnostic and therapeutic targets .

The PIN module integrated into AutDB is licensed to Simons Foundation as SFARI Gene and is available at https://gene.sfari.org/autdb/PINHome.do .

**157.061** No Evidence of Excess of De Novo Mutations in Autistic Children from Multiplex Families. C. L. Simpson*[1], Y. Kim[2], C. A. Wassif[3], N. Hansen[1], J. Mullikin[1], E. Tierney[4], F. D. Porter[3] and J. E. Bailey-Wilson[1], (1)*National Human Genome Research Institute, National Institutes of Health*, (2)*Food and Drug Administration*, (3)*National Institute of Child Health, National Institutes of Health*, (4)*Kennedy Krieger Institute*

Background: The presence of an excess of *de novo* single nucleotide variants (SNVs), insertion/deletion (INDEL) and copy number variants (CNVs) has been widely reported in the analysis of exome sequencing in families with a single affected child (simplex families). The overall picture remains unclear as to whether there is a general excess of de novo variants or whether the increase in frequency is particularly marked in gene-disrupting mutations. In addition, it is not known if this excessive mutation rate is also observed in families with 2 or more affected children (multiplex families).

Objectives: We aimed to investigate whether affected probands and affected siblings in multiplex families showed an excess of *de novo* mutations compared to the overall mutation rate in unaffected children.

Methods: We performed whole exome sequencing in 124 individuals from 26 families with 2 or more

affected children (range 2-3) from the Autism Genetic Resource Exchange (AGRE). Poorly performing variant calls were identified and removed in Golden Helix SVS. Variants which caused Mendelian errors in SNV and INDEL variants were identified using PLINK. Error rates for the offspring in each pedigree were calculated in R and compared both within and across families using a T test.

Results: Two families were removed from the analysis due to incomplete sequencing at the time of analysis or sample identity mismatches leading to incomplete family data. There were 49 affected and 22 unaffected offspring. After quality control measures to remove poor quality calls in both the SNVs and INDELs, 2.2% of all variants were inconsistent in at least one independent pedigree. Of the inconsistent variants, 15.1% of SNVs and 22.7% of INDELs generated Mendelian errors in more than one pedigree. These variants were removed as probable sequencing artifacts before analysis. In the remaining data, there were 440902 SNVs and 62262 INDELs. For the SNVs, the mean Mendelian error rate in affected offspring was $5.9x10^{-5}$ (range $9.1x10^{-6}$ to $4.2x10^{-4}$) and the mean rate for unaffected offspring was $4.1x10^{-5}$ (range $1.1x10^{-5}$ to $1.7x10^{-4}$). In the INDELs, the mean Mendelian error rate for affected offspring was $1.5x10^{-4}$ (range $4.8x10^{-5}$ to $4x10^{-4}$) and for unaffected offspring the mean rate was $1.1x10^{-4}$ (range 0 to $2.4x10^{-4}$). Affected individuals did not show markedly higher rates of Mendelian inconsistency than unaffected individuals in SNVs (p=0.2) or INDELs (p=0.06).

Conclusions: Although *de novo* mutations have been reported as important in families with a single affected child, these families with multiple affected children do not seem to show this same pattern of excessive *de novo* variants in affected compared to unaffected individuals. In addition, some of the observed inconsistencies were seen in multiple independent pedigrees, suggesting that these are sequencing artifacts rather than genuine *de novo* mutations. Even in the possible *de novo* variants observed in only a single pedigree, it is likely that some of these will also be artifact. Work is ongoing to examine whether the pattern of *de novo* variants in cases is clustered more in gene disrupting mutations compared to unaffected individuals in these families.

**157.062 62** The Etiological Relationship Between Dimensional Traits and Categorical Diagnostic Constructs of ASD. B. Tick*[1], E. Colvert[2], F. Rijsdijk[3], E. L. Woodhouse[4], F. McEwen[5], F. Happe[2] and P. F. Bolton[2], (1)*SGDP, IoP, King's College London*, (2)*King's College London*, (3)*Institute of Psychiatry, KCL*, (4)*Institute of Psychiatry, King's College London*, (5)*SGDP, Institute of Psychiatry*

Background: Evidence from twin and family studies to date has shown that liability to autism impairments in social communication and interest patterns extends beyond the traditional categorical diagnostic boundaries, thus leading to broadening of diagnostic criteria to include other developmental subtypes. The Autism Spectrum Disorder diagnosis was therefore re-conceptualised as the extreme end of dimensionally distributed set of autistic traits in the population, rather than a separate behavioural entity. Most recent twin studies further confirmed that the genetic factors responsible for the variation of autism trait scores in the population are likely to be the same for the extreme trait scores at the end tail of the same distribution.

Objectives: To define the relative genetic (A), shared (C) and unique (E) environmental influences on the hypothetical overlap between the continuous measure of autism traits (Children Autism Spectrum Test, CAST) in a large population of UK twins and a sub sample of the same cohort in which at least one twin has received a clinical diagnosis of Broad Spectrum or ASD, assessed by DAWBA/ADOS/ADI-R and an overall Consensus Diagnosis (CD). Additionally, we wanted to validate findings of a recent study reporting the importance of shared (C) environmental influences (Hallmayer et al, 2011) in clinical autism/ASD diagnosis.

Methods: The genetic and environmental parameters were estimated in a bivariate continuous-ordinal liability threshold model. To account for the selected nature of the sample the thresholds were fixed to 'known' population z-values: the 1st threshold discriminating between categories 0 and 1 was fixed at 5% (Broad Spectrum) and the 2nd threshold discriminating between 1 and 2 was set to 1% (ASD).

Results: Cross-twin within-trait correlations for CAST, ADOS and CD indicated no role of shared environment (C), except for ADI-R; whereas dominant rather than additive genetic effects were indicated for the DAWBA. The cross-twin cross-

trait correlations between CAST and ADI-R, ADOS and CD all indicated mainly genetic and unique environmental influences on the covariance. The phenotypic overlap ($r_{ph}$) between CAST and all clinical measures were moderate to high (.52 to .65) and mostly influenced by genes ($r_{ph}$-A for DAWBA=.40, ADI-R=.58, ADOS=.56 & CD=.60) and the remainder explained by unique environments ($r_{ph}$-E: DAWBA=.12, ADI-R=.03, CD=.05) but not significantly so for ADOS ($r_{ph}$-E=-.02). No shared environmental factors acted on the covariance between CAST and clinical measures.

Conclusions: In the first study of this kind, we revealed a phenotypic overlap between continuous and ordinal measures of autistic traits and ASD and that this is largely due to genetic factors.

## 158 Intellectual and Behavioral Assessment and Measurement

**158.063 63** Calibrated Severity Scores for the Autism Diagnostic Observation Schedule-Toddler Module. A. N. Esler*[1], V. Hus Bal[2], W. Guthrie[3] and C. Lord[4], (1)*University of Minnesota*, (2)*University of Michigan*, (3)*Florida State University Autism Institute*, (4)*Weill Cornell Medical College*

Background: Calibrated severity scores have been created for Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2) as a metric of the relative severity of autism-specific behaviors, as measured by this instrument (Gotham, Lord, & Pickles, 2009). Calibrated severity scores are available for modules 1-3 and soon will be available for module 4. The goal was to create a standardized score to compare autism symptoms within and across individuals, independent of age and developmental level. Calibrated severity scores for modules 1-3 had more uniform distributions across age and developmental level and were less influenced by demographic variables than ADOS-2 raw totals. A comparable metric is not yet available for the ADOS-2 Toddler Module (ADOS-T), used to assess toddlers between 12 and 30 months of age.

Objectives: Standardize ADOS-T raw scores to approximate a metric of ASD-related symptom severity that is less influenced by developmental level, age, and other demographic variables.

Methods: Analyses were conducted using ADOS-T and psychometric data for 360 children with ASD age 12 to 30 months, some with repeated assessments for a total of 823 cases. Following procedures informed by Gotham and colleagues (2009), the ASD sample was divided into groups based on chronological age and language level. Within each group, raw scores were mapped onto a 10-point severity metric, using percentiles of raw totals corresponding to ADOS-T classifications.

Results: Distributions of severity scores showed increased comparability across the age/language groups compared to raw totals. Multiple linear regression analyses were performed separately for calibrated severity score and raw total to examine whether participant characteristics such as age and IQ would be less associated with severity scores than with raw scores. Only verbal IQ was a significant predictor for both raw total and calibrated severity scores. While verbal IQ accounted for 33% of the variance in ADOS-T raw totals, it accounted for only 19% of the variance in severity scores.

Conclusions: ADOS-T calibrated severity scores demonstrated reduced associations with verbal IQ. For modules 1-3, severity scores have demonstrated usefulness creating more homogeneous groups for clinical, genetic, and neurobiological research. The addition of ADOS-T calibrated scores allows comparisons to be made starting at 12 months, expanding the ability to identify trajectories of ASD symptoms potentially at the first signs of concern. Future studies should replicate calibrated severity scores in large independent samples. ADOS-T severity scores should be evaluated for validity in predicting outcomes (e.g., eventual ASD diagnosis, response to intervention).

**158.064 64** Abnormal Vestibulo-Ocular Reflexes in Autism Spectrum Disorders. B. Wilkes*[1], T. B. Carson[1], J. H. Ko[2], J. W. Bodfish[3], K. M. Newell[2] and M. H. Lewis[1], (1)*University of Florida*, (2)*Pennsylvania State University*, (3)*Vanderbilt University*

Background: Although not diagnostic for the disorder, altered sensory-motor function has been frequently observed in children with ASD. Some of these alterations (e.g., decreased postural stability, altered vestibulo-ocular reflexes) depend upon adequate processing of vestibular sensory input. The rotational vestibulo-ocular reflex (rVOR), which functions to maintain stable vision by generating compensatory oculomotor responses to angular rotation head movements, may be useful for studying vestibular related

sensory motor processing in ASD. The primary measures of the rVOR (time constant of decay, gain, symmetry) provide information about the functional ability of peripheral vestibular anatomy or central processing of vestibular sensory information. Abnormalities in rVOR beyond these standard measures have been noted, but not systematically studied, in children with ASD. rVOR eye movements are composed of nystagmus beats (i.e., slow phase eye excursions followed by a quick phase reset to center), that occur during and after continuous whole body rotation in the earth-horizontal plane. Typical horizontal nystagmus occurs in a linear and periodic fashion, without vertical or torsional intrusions.

Objectives: The primary objective of the present study was to investigate differences in the temporal dynamics of rVOR between ASD and typically developing children using video-oculography techniques.

Methods: Children diagnosed with ASD (n=15) and typically developing (TD) children (n=16) ages 6-12 matched on age, sex, and IQ participated in the study. Rotary chair testing was completed using a computer-controlled, motorized rotary platform and binocular video-oculography goggle (VOG) system (Neuro-Kinetics). Post rotary rVOR eye movements were recorded for 30-50 seconds in the dark with eye position sampled at 100 Hz. Eye movement tracings during the first 20 seconds that followed cessation of rotation were evaluated using time series models (Approximate Entropy and spectral analysis) designed to assess regularity or periodicity in eye position.

Results: Children with ASD exhibited rVOR eye movements that differed markedly from TD children. Visual inspection of eye position tracings of TD children showed the expected horizontal, periodic eye movements whereas those of ASD children were markedly irregular. Moreover, unlike TD children, ASD children showed numerous vertical eye movements. Quantitative measures of regularity or periodicity (ApEn, spectral analysis) confirmed these group differences.

Conclusions: Beyond changes in standard measures of rVOR, ASD children exhibited clear differences in post-rotary nystagmus. The marked irregularity of horizontal nystagmus and novel identification of frequent vertical intrusions suggest cerebellar deficits. Vertical intrustions exhibited by ASD children likely disrupted the regularity or periodicity of horizontal nystagmus. If rVOR alterations are selective for ASD, this reflex which can be measured in infants, could be a potentially important early biobehavioral marker in ASD.

**158.065 65** Clinical Application and Validation of the Autism Detection in Early Childhood (ADEC) in Referred Children Aged 14-36 Months in a US Pediatric Hospital. D. Hedley*[1], R. E. Nevill[2], Y. Monroy Moreno[3], B. Murphy[1], N. Fields[2], J. Wilkins[1], J. A. Mulick[2] and E. Butter[1], (1)*Nationwide Children's Hospital*, (2)*The Ohio State University*, (3)*National Autonomous University of Mexico*

Background: In the USA early diagnosis of Autism Spectrum Disorder (ASD), and hence access to timely intervention, is often hampered by long wait lists for diagnostic services. Improved screening may reduce wait times by limiting the number of referrals of children who do not go on to receive an ASD diagnosis. Children suspected of ASD typically present at clinics that also serve children with suspected language, intellectual, developmental, and/ or behavior problems. Differentiating ASD from other diagnoses can, however, prove extremely challenging. For example, a study conducted by the Cincinnati Children's Hospital Medical Center found the Autism Diagnostic Observation Schedule (ADOS), considered to be the current "gold-standard" test for autism diagnosis, returned specificity of only 29%, although sensitivity was better at 76-99% (Murray et al, 2010). Furthermore, poor specificity of the ADOS in this population could potentially contribute to over diagnosis. The challenge is to develop effective instruments for use in "real life" clinical settings. In the present study we evaluated the Autism Detection in Early Childhood (ADEC), a brief, play-based screening tool designed to identify at-risk children aged 12-36 months which can be implemented with minimal training. The ADEC has yet to be evaluated in the USA.

Objectives: To evaluate the clinical utility of the ADEC as an ASD screening tool in children at risk of ASD who were referred to a hospital developmental clinic.

Methods: Children (*n* = 57) aged 14-36 months presenting at the developmental disabilities clinic of a large Midwestern pediatric hospital for diagnostic evaluation were assessed with the

ADEC. ADEC administrators trained to maintain coding reliability were blind to the outcome of the child's intake interview and all subsequent developmental assessments, and all clinical personnel were blind to ADEC scores. Children suspected of ASD (*n* = 31) by the diagnostic clinician were assessed by an interdisciplinary team consisting of a speech language pathologist, psychologist, and developmental behavioral pediatrician or pediatric neurologist using *DSM-5* diagnostic criteria. The appropriate ADOS-2 module was administered by research-trained psychometricians. For the remaining children, ASD had been ruled out by the initial clinician and they were typically referred for non-ASD assessments (*n* = 26). Twenty-two children received a diagnosis of ASD. Other diagnoses included developmental delay, coordination, language and behavior disorders.

Results: Sensitivity for the ADEC was 100% and specificity was 71%, both for the full sample and when limiting analysis to children referred for an interdisciplinary ASD assessment. PPV ranged from 69-86% and NPV was 100%. Inter-rater reliability for 30 dual-coded (video or live) administrations was ICC = .96. Cohen's kappa for individual items ranged from .56 - .90. Internal consistency was Cronbach's alpha = .78.

Conclusions: The ADEC was found to be psychometrically sound and compared favorably with the ADOS-2 in predicting final diagnosis using current diagnostic criteria. Our preliminary findings suggest that the ADEC has the potential to contribute valuable information during initial screening, which may help to reduce wait lists for targeted diagnostic assessments and facilitate earlier access to appropriate services.

**158.066 66** Population-Based Screening for Autism Spectrum Disorder Using the Social Communication Questionnaire. L. A. Carpenter*, C. C. Bradley, A. E. Wahlquist, J. Charles, W. Jenner, A. P. Cohen, H. Specter and L. B. King, *Medical University of South Carolina*

**Background:** The Social Communication Questionnaire (Rutter, Bailey, and Lord, 2003) is a 40-item checklist designed to identify children who may be at risk of having autism spectrum disorder (ASD).

**Objectives:** To describe the distribution of SCQ scores in a population of school aged children (8 years of age) from a racially and economically diverse area in South Carolina (SC).

**Methods:** The South Carolina Children's Educational Surveillance Study (SUCCESS) is an ongoing population-based study that will determine the prevalence of Autism Spectrum Disorder (ASD) among a population of children born in 2004 and living in one of three counties surrounding Charleston, SC. The region is racially and economically diverse (59% White, 32% Black, 7% Hispanic, and 2% other; 33% schools with Title 1 status). The SCQ was distributed to parents of eligible children in approximately half of the public and private schools in the catchment area (the study is in progress in the remaining schools). Ongoing efforts have been made to reach home-schooling families through community outreach and home-school associations. Rate of participation in the screening phase for the first three waves (out of six planned waves) of the study varied by school and ranged from 22%-100% (overall response rate thus far = 51%). Schools with low response rates (<50%) are currently being targeted with special interventions to improve responding.

**Results:** In the first three waves of the SUCCESS study (n = 1498), 2.2% of youth were at very high risk for ASD (SCQ>21); 5.41% were at risk (SCQ 15-21); and 20.83% fell just below the threshold for risk on the SCQ (SCQ 8-14). Males were more likely to score in the at-risk range than females ($x^2$=6.87, p=0.009). Minority children had a higher average SCQ score than white children, and were more likely to be identified as being at-risk for ASD ($x^2$=5.91, p=0.015). Hispanic children were also more likely to be identified as being at-risk compared to non-Hispanic children ($x^2$=8.31, p=0.0039). In addition, children attending Title 1 schools (those with a high percentage of low-income students) also had higher average SCQ scores and were more likely to be at risk for ASD than those children not attending a Title 1 school ($x^2$=43.7, p<0.0001).

**Conclusions:** Almost 8% of 8-year-old children in this general population sample were identified as being at-risk for ASD. Males, minority children, and children attending low-income schools had higher average SCQ scores, and were more likely to be identified as being at risk for ASD Further evaluation is needed to determine if these

increases accurately reflect higher ASD risk in these populations or if these differences can be accounted for by differential responding or measurement artifacts on the SCQ. Future SUCCESS efforts will address these issues through the completion of screening, and ongoing diagnostic evaluations of approximately 10% of the sample in order to establish the prevalence of ASD in the study area, compare DSM-IV and DSM-5 diagnoses, and determine the sensitivity and specificity of the SCQ as a screening instrument for ASD in population-based samples.

**158.067 67** Associations Between Handwriting Fluency and Motor Control in Children with Autism. B. Dirlikov*[1], S. H. Mostofsky[2], A. J. Bastian[3] and M. B. Nebel[2], (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins School of Medicine*, (3)*Johns Hopkins School of Medicine, Kennedy Krieger Institute*

Background: Children with ASD experience difficulty performing a host of skilled motor behaviors, including handwriting. Children develop automaticity in handwriting which reduces interference of motor demands with higher-order cognitive processes related to composition. Therefore, the dynamics of writing account for a large portion of variance in composition fluency.

Objectives: To use advanced mathematical modeling to compare handwriting performance under different demands and relate handwriting to measures of motor and cognitive function.

Methods: Writing performance was assessed using a digitizing tablet (Wacom Intuos4) in 56 children, 20 with ASD (17M and 3F) and 36 typically developing (TD; 29M and 7F), ages 8-12 years. Groups were balanced for age, gender, IQ (PRI), and SES. Each participant completed a handwriting task in which they copied and traced 6 non-latin alphabet characters. Letter speed and form, as well as speed inflections were extracted using Matlab. Letter Form was analyzed using LDDMM to map shape morphometry. Spectral power (SP) was also assessed using Fourier transform on the velocity curve for each letter.

Results: Repeated measures ANOVA revealed a significant effect of diagnostic group for Letter Form ($F=7.88$, $p=.007$), Speed ($F=4.65$, $p=.036$), and Speed Variability ($F=13.17$, $p=.001$), with TD performing better/slower than ASD for all measures. An effect of condition (better when tracing) was significant across diagnostic groups for Letter Form, Speed, and Speed Variability ($F>29.28$, $p<.001$). A significant groupxcondition interaction effect was only seen for Letter Speed ($F=4.65$, $p=.036$). Post-hoc tests revealed significant group (TD>ASD) differences in both conditions for Letter Form (Copy: $F=3.89$, $p=.05$; Trace: $F=13.78$, $p<.001$) and Speed Variability (Copy: $F=6.07$, $p=.017$; Trace: $F=10.64$, $p=.002$). Letter Speed showed group differences (ASD>TD) only in the Copy condition (Copy: $F=6.71$, $p=.012$; Trace: $F=.351$, $p=.556$). SP analysis revealed significant increases in 4 and 5Hz frequency bins for children with ASD in the Copy condition only (4Hz: $F=12.53$, $p=0.001$; 5Hz: $F=8.84$, $p=.005$). Pearson's correlations revealed significant correlations between Letter Form and Working Memory Index (WISC-IV) in the ASD group, particularly during the Copy condition (Copy: $r=-0.72$, $p<0.001$; Trace: $r=-0.45$, $p=0.046$). Four hertz SP was significantly correlated with mABC-2 Aiming and Catching standard score ($r=-.58$ $p=0.008$) during the copy condition. Significant correlations were not observed for the TD group.

Conclusions: These results provide further evidence that children with ASD have substantial difficulties with handwriting, manifested as poor letter formation and fluency. Tracing resulted in improvements in letter formation, speed, and variability in both groups, and was particularly advantageous for normalizing speed in children with ASD. Analysis of speed variability revealed that children with ASD showed increased 4-5Hz periodicity when copying, which has previously been associated with cerebellar impairments. For children with ASD, letter formation was associated with working memory particularly during copying suggesting that difficulty maintaining the visual representation of the letter during motor preparation may contribute inaccuracies in the formation of letters. Further, increased 4-5Hz periodicity was associated with poorer aiming and catching in children with ASD, suggesting that impairments in visual-motor integration, perhaps at the level of the cerebellum, contribute to poor writing fluency.

**158.068 68** Attenuation but Persistence of Normative Sex Differences in Empathizing, Systemizing, and Autistic Traits in 800 High-Functioning Adults with Autism: A Big-Data Test of the 'Extreme Male Brain' Theory. S. Baron-Cohen*, S. A. Cassidy, B. Auyeung, C. Allison, M. Achoukhi, S. Robertson and M. C. Lai, *University of Cambridge*

Background: Sex differences have been reported in autistic traits, empathizing and systemizing among typical individuals. In individuals with autism, these cognitive-behavioural profiles correspond to predictions from the 'extreme male brain' (EMB) theory of autism. Sex differences within autism, however, have been under-investigated.

Objectives: This study aims to examine sex differences using self-report measures of empathizing, systemizing and autistic traits in a large sample of individuals with autism, in order to have sufficient power to test if sex differences exist within autism and if these are attenuated as would be predicted by the EMB theory

Methods: n = 811 adults (454 females) with autism were compared with 3,906 age-matched typically developing adults (2,562 females). Participants completed the Empathy Quotient (EQ), the Revised Systemizing Quotient (SQ-R) and the Autism Spectrum Quotient (AQ) online. The discrepancy between standardized EQ and SQ-R scores (the 'D-score') was also used to classify individuals into different cognitive-behavioral profiles ('brain types').

Results: Typical females on average scored higher on the EQ, and typical males scored higher on the SQ-R and AQ, confirming earlier studies. Both males and females with autism showed a shift toward the extreme of the 'male profile' on these measures and in the distribution of 'brain types'. There were sex differences in the autism group on the AQ, EQ, SQ-R and D scores, though smaller compared to those observed in the typically developing group, all evidenced by a significant ordinal sex-by-diagnosis interaction. Normative patterns of sex differences were preserved in the autism group for all the measures, evidenced by significant differences between males and females with autism.

Conclusions: In a large sample of high-functioning adults with autism, both males and females cognitive-behavioural profiles of empathizing, systemizing, and autistic traits show a shift towards and beyond the typical male range of scores. However, normative sex differences were preserved in individuals with autism, highlighting significant differences between males and females with autism. This exemplifies that the presence of autism attenuates but does not eliminate typical sex differences in these aspects of cognitive-behavioral traits.

**158.069 69** A Novel Severity Measure for Quantitative Description of Heterogeneity in Autism. B. Tunc*[1], Y. Ghanbari[1], A. R. Smith[1], J. Pandey[2], A. N. Browne[2], R. T. Schultz[1] and R. Verma[1], (1)*University of Pennsylvania*, (2)*The Children's Hospital of Philadelphia*

Background: The evaluation of individuals with ASD is usually assessed by phenotypic scores describing different aspects of the clinical presentation. ASD heterogeneity, however, makes detection of differences between affected individuals and typically developing controls (TDCs) difficult when phenotypic measures are imprecise and lead to overlap for ASD and TDC samples. Many research applications would benefit greatly from a continuous severity measure to characterize the impact of specific etiologically significant factors, including genetic risk variants and brain processes captured by neuroimaging data.

Objectives: The aim of this work is to design a severity measure that quantifies individual differences in the autism spectrum by fusing information from various phenotypic scores that describe different aspects of functioning, when individually none provide a complete characterization. The validity of the measure will be tested for its ability to categorize sample differences in diffusion tensor brain imaging data.

Methods: A dataset of 370 male subjects with ASD and 118 male TDCs was collected. From a large battery of measures, 50 key phenotypic scores were chosen for the analyses. The individual severity belief of a score was estimated from the cumulative distribution function of the score defined over the ASD sample. The weighting of these individual decisions was established based on the average classification error between ASD and TDC when using these scores. Probabilistic voting was used to fuse individual decisions of different phenotypic scores in a weighted manner. The measure was used to determine groups of high and low severity in the population. These subgroups were then used to study imaging-based group differences on DTI data acquired with 30 gradient directions. Fractional anisotropy (FA) maps computed from the DTI data.

Results: When the ASD sample is stratified according to this severity measure, voxel-wise analysis of the FA maps revealed differences that could not be seen when the sample was analyzed as a whole. Regions of differences agree with previous diffusion-based studies in ASD. Several regions, including the body of corpus callosum, corona radiate, superior longitudinal fasciculus and the inferior fronto-occipital fasciculus show significant group differences only when TDCs are compared to the more severe tail of the ASD distribution that is defined by this severity measure. These results are compared to stratification by a traditional dimensional measure of ASD – the Social Responsiveness Scale (SRS), which focuses on the core diagnostic symptoms. By fusing a broad range of scores, many of which are ancillary to the core of ASD, this new severity metric performs as well or better.

Conclusions: We have designed a severity measure that combines information from individual phenotypic scores to define a measure of heterogeneity. It does better in detecting TDC vs ASD differences than any single test scores. DTI-based imaging analysis of groups selected based on this severity score revealed larger differences between ASD and TDC samples.

**158.070 70** Emotion Dysregulation in Children and Adolescents with Autism Spectrum Disorder. A. C. Samson*[1], A. Y. Hardan[2], J. J. Gross[1], J. M. Phillips[2], Y. Arbab[1] and R. W. Podell[3], (1)*Stanford University*, (2)*Stanford University School of Medicine*, (3)*Teachers College, Columbia University*

Background: Although not being a core feature of Autism Spectrum Disorder (ASD), parents and clinicians have long noted the importance of emotion dysregulation in individuals with ASD (e.g., tantrums, meltdowns).

Objectives: The aim of the present study was to examine emotion dysregulation in children and adolescents with ASD, with a special focus on cognitive reappraisal, which involves thinking differently about an event in order to feel less negative.

Methods: Twenty-one high-functioning children and adolescents with ASD (mean age: 12.71 years, SD=3.62) and 22 gender- and age-matched typically developing (TD, mean age: 13.00 years, SD=2.99) controls completed the Reactivity and Regulation Situation Task (Carthy et al., 2010). This task assesses first emotional reactivity and spontaneous use of emotion regulation strategies (problem solving, cognitive reappraisal, avoidance, distraction, venting, suppression, and relaxation) in the context of ambiguous and potentially threatening negative scenarios. After the concept of cognitive reappraisal was explained, the scenarios were presented again, and the participants were prompted to use this strategy.

Results: Individuals with ASD exhibited the same level of reactivity to negative stimuli as TD participants. Furthermore, youth with ASD had a different emotion regulation profile than TD individuals, characterized by using cognitive reappraisal less frequently and by using suppression more frequently. When prompted to use cognitive reappraisal, participants with ASD were less able to implement, but benefitted from this strategy when they were able to generate a reappraisal.

Conclusions: Findings suggest that cognitive reappraisal may be useful to individuals with ASD. Therefore, the development of treatments that focuses on enhancing the use of adaptive forms of emotion regulation might decrease emotion dysregulation and optimize long-term outcomes in youth with ASD.

**158.071 71** Behavioral Evidence of Hemispheric Disconnectivity in Autism Spectrum Disorders. C. Jung*[1] and J. J. Hutsler[2], (1)*University of Nevada, Reno*, (2)*University of Nevada Reno*

## Behavioral Evidence of Hemispheric Disconnectivity in Autism Spectrum Disorders

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Background: Long-range underconnectivity has been implicated as an underlying cause of cognitive and behavioral deficits associated with autism spectrum disorders (ASD). In ASD, long-range underconnectivity has been shown to affect the dynamics of brain synchronization during complex cognitive tasks, such as coordinating motor activity and achieving a cohesive experience of the sensory world (Frith 2003; Just et al. 2004). Interhemispheric transfer is one route of long range communication within the brain, and patient populations characterized by

diminished interhemispheric connectivity have demonstrated distinct patterns of reaction time and accuracy in stimulus-response tasks. Individuals with agenesis of the corpus callosum and callosotomy benefit more from the presentation of bilateral stimuli compared to unilateral stimuli (Roser and Corballis 2003). This *redundancy gain* results in faster reaction times to bilateral stimuli in these disorders, but not in neurotypical subjects. The integrity of interhemispheric transfer can also be assessed by presenting conflicting stimuli to each visual field and determining processing performance. Neurotypical groups struggle to process competing information due to task interference, while patients without a corpus callosum are not affected by this increased *perceptual load* (Holtzman and Gazzaniga 1985). If impaired long-range connectivity is a characteristic of ASD, interhemispheric transfer abnormalities, such as enhanced redundancy gain and resilience to increasing perceptual load, may be observed in this population.

Objectives: To understand the impact of long-range underconnectivity on behavioral performance in ASD, we employed two experimental paradigms that have been used to evaluate other disconnectivity syndromes. In the first, we examined redundancy gain, and in the second, we tested the effects of increased perceptual load on task performance.

Methods: 12 high-functioning ASD boys between the ages of 6-17 and 13 age-matched neurotypical (NT) controls were instructed to indicate with a key press whenever they saw a unilateral or bilateral stimulus appear. Reaction times were evaluated by trial type and subject group. Participants then observed simultaneously presented animated patterns in both visual fields. Patterns were either the same (redundant) or different (mixed) and, after a delay, subjects had to indicate whether a third lateralized pattern matched that which was presented in the same visual field.

Results: As predicted, NT subjects' reaction times did not differ when exposed to simple unilateral and bilateral stimuli. In contrast, ASD subjects were faster to respond to bilateral stimuli relative to unilateral stimuli. In the second study, neurotypicals were less accurate at correctly identifying the mixed patterns relative to the redundant patterns. In contrast, the performance of ASD subjects was not affected by the increased perceptual load required for evaluating mixed patterns.

Conclusions: ASD subjects demonstrate patterns of behavioral performance in both tasks that are essentially equivalent to those found in patients with corpus callosum deficiencies. The greater redundancy gain exhibited in the ASD group implies compromised processing efficiency for lateralized information, while their performance on tasks with increasing perceptual load demonstrates greater isolation between the hemispheres

**158.072 72** Behavioral and Cognitive Characteristics of Females and Males with Autism in the Simons Simplex Collection. R. Embacher*[1], T. W. Frazier[2], S. Georgiades[3], S. L. Bishop[4] and A. Y. Hardan[5], (1)*Cleveland Clinic Children's Hospital*, (2)*Cleveland Clinic*, (3)*Offord Centre for Child Studies & McMaster University*, (4)*Center for Autism and the Developing Brain, Weill Cornell Medical College*, (5)*Stanford University School of Medicine*

Background: Being male is one of the most powerful and well-established risk factors for autism spectrum disorders (ASD). Sex ratio estimates have indicated 3-4 males per female across the diagnostic spectrum. Even more severe ratios (as high as 9:1) are observed in cognitively higher functioning cases. Consequently, original descriptions, subsequent diagnostic criteria, and the vast majority of phenotypic data are from males with ASD. Yet, recent data suggest that females may be under-identified or, at minimum, show a different behavioral expression of autism. Unfortunately, studies of sex differences in the ASD phenotype have often included modest female sample sizes and/or focused on a limited number of domains (e.g. symptoms or cognition). The Simons Simplex Collection affords the advantage of simultaneously evaluating an array of phenotypic measures, including core ASD symptoms, cognitive and language measures, adaptive functions, and associated behavior problems in a large number of females and males with ASD.

Objectives: The primary aim was examine differences in behavioral symptoms and cognitive functioning between males and females with ASD. The secondary aim was to determine whether sex differences in IQ explained sex differences in other domains. The tertiary aim was to evaluate

whether measurement differences between sexes for autism symptoms may be driving sex ratios for ASD diagnosis.

Methods: We analyzed data from 2418 probands with autism (304 females, 2114 males) included in the Simons Simplex Collection. Sex differences were evaluated across measures of autism symptoms, cognitive and motor functioning, adaptive behavior, and associated behavior problems. Measurement bias was examined using multi-group confirmatory factor models of autism symptom measurements. Unadjusted and propensity-adjusted analyses were computed to ensure sex differences were not due to unbalanced sampling. Moderator and mediator analyses evaluated whether sex differences were modified by clinical characteristics or driven by cognitive ability.

Results: Females with ASD had significantly greater social communication impairment, lower levels of restricted interests, lower cognitive ability, weaker adaptive skills, and greater externalizing problems relative to males. All effect sizes were small to moderate (Cohen's d<=.22) but still potentially clinically meaningful. Sex differences tended to be larger at older ages (largest p=.045). IQ reductions mediated greater social impairment and reduced adaptive behavior in females with ASD, but did not mediate reductions in restricted interests or increases in irritability. Symptom differences could not be accounted for by measurement differences, indicating that diagnostic instruments captured autism similarly in males and females.

Conclusions: A specific female ASD phenotype is emerging that cannot be accounted for by differential symptom measurement. The present data suggest that the relatively low proportion of high functioning females may reflect the effect of protective biological factors or may be due to under-identification. Additional carefully-accrued samples are needed to confirm the present pattern and to evaluate whether observed sex ratios in high functioning cases are reduced if female-specific indicators of restricted interests are included.

**158.073 73** Cognitive Ability Is Associated with Different Outcome Trajectories in Autism Spectrum Disorders. E. Ben Itzchak*[1], L. R. Watson[2] and D. A. Zachor[3], (1)*Ariel University*, (2)*University of North Carolina*, (3)*Tel Aviv University / Assaf Harofeh Medical Center*

Background:

Children with autism spectrum disorder (ASD) comprise a highly heterogeneous group with great variability in clinical expressions and in intervention outcome. Some achieve marked progress in development, while others achieve only modest or no significant gains. One of the most reported predictors of outcome in ASD that can explain this variability in outcome is the baseline cognitive ability. Most of the follow-up studies in ASD looked at outcome at a single time point after 1-2 years of intervention and only a few compared developmental gains after the first versus the second year of treatment.

Objectives:

1. To compared outcomes in autism symptoms severity and adaptive skills after the first versus the second year of early intensive behavioral intervention (EIBI). 2. To further look at the impact of the cognitive ability at baseline on outcome trajectories in these domains in these two time periods.

Methods:

The study included 46 participants, 39 boys and 7 girls, (mean age=25.5m, SD=3.95, age range 17 to 33 months) diagnosed with ASD. All participants completed three assessments, at diagnosis (T1), after one year (T2) and two years (T3) of center-based EIBI. The entire group was divided according to the median of the DQ composite scores (70 points) into a higher cognitive (HC≥70) group and a lower cognitive (LC<70) group. Outcome was assessed in autism symptoms severity using the Autism Diagnostic Observation Scales (ADOS) severity scales and in adaptive skills using the Vineland Adaptive Behavior Scales (VABS).

Results:

The entire group showed a significant decrease in autism severity scale scores from T1 to T3. Significant improvement in the social-affect domain was noted during the first intervention year, whereas the restricted repetitive behaviors severity scores declined gradually during the entire period. No significant Time X Group interaction was found, meaning that the two cognitive groups did not significantly differ in their intervention outcome trajectories in those

measures. Regarding adaptive skills, a different trajectory for the two cognitive groups was noted (Time X Group interaction, p <.05). Only the HC group showed significant increase in the communication (p<.001), but only in the first year (p<.01)], in daily living skills (p=.003), and in socialization (p=.002) but only in the second year. A decline in motor skills domain was significant for both groups in the first year (p<.001). The LC group maintained but did not increase their adaptive skills standard scores level over time.

Conclusions:

The two cognitive groups acquired more typical social-communication skills and showed decrease in the stereotypic behaviors. However, having a higher baseline cognitive level seemed to enable the incorporation of the new acquired socio-communication skills better in daily life. Having lower cognitive ability at baseline was still associated with acquisition of new adaptive skills with time, but prevented the marked progress seen in children with higher cognition. As some of the examined skills were improved only after the second year of intervention, it may accentuate the importance of continuing intensive intervention in ASD. Future long-term studies should highlight other potential moderators of outcomes.

**158.074 74** Comparing the Performance Characteristics of ASD Screening Measures in Toddlers. A. L. Palmer*, A. Vehorn and Z. Warren, *Vanderbilt University*

Background: Although there has been growing emphasis on early screening and detection of ASD, the average age of diagnosis in the U.S. still remains between 4 and 5 years of age (CDC, 2012). In an effort to lower the age of diagnosis and take advantage of early intervention services, the American Academy of Pediatrics recommends universal screening for ASD beginning at 18 months of age. The most widely used screening measure, the Modified Checklist for Autism in Toddlers (M-CHAT), has been shown to identify many children with ASD at young ages, but often results in substantial over-identification of children with other developmental concerns particularly when clinicians do not utilize the embedded follow-up interview or other validation procedures (Chlebowski et al., 2013; Miller et al., 2011). This over-identification is particularly problematic given that most tertiary assessment centers struggle to provide diagnostic assessment without substantial waits.

Objectives: To determine if a new screening instrument, the Vanderbilt Scales for ASD, utilizing graded parental ratings of early core symptoms of ASD, would possess improved performance characteristics over the M-CHAT in accurately identifying children with and without ASD. The Vanderbilt Scales for ASD consists of 23 items. These items were pulled from developmental checklists and interviews commonly used at Vanderbilt clinics. Those items with the highest weights, determined by a standardized canonical function, were chosen to be included in the Vanderbilt Scales. We also investigated the incremental clinical value of use of a structured observation of behavior in conjunction with the parent report screening measures.

Methods: Participants included 161 children, ages 36 months or younger, participating in first-time diagnostic appointments or autism research protocols at a university based autism clinic. Examined measures included the M-CHAT, Vanderbilt Scales for ASD, and Autism Diagnostic Observation Schedule (ADOS). Three items from the ADOS that could potentially be easily administered by community clinicians were chosen as a structured observation of behavior. Sensitivity, specificity, and PPV were calculated for each screening measure as well as the simultaneous testing of each screening measure with the three ADOS items.

Results: Reliability analysis of the Vanderbilt Scales for ASD yielded a cronbach's alpha of .803. A cutoff score of 9 on the Vanderbilt Scales resulted in sensitivity= 80.65%, specificity= 66.18%, and positive predictive value= 76.53%. M-CHAT: sensitivity= 87.10%, specificity=52.94%, and positive predictive value= 71.68%. Screen positive on both the Vanderbilt Scales and ADOS items: sensitivity= 77.22%, specificity= 86.54%, and positive predictive value= 89.71%. Screen positive on both the M-CHAT and ADOS items: sensitivity= 75.28%, specificity= 83.61%, and positive predictive value= 87.01%.

Conclusions: The Vanderbilt Scales was slightly less sensitive than the M-CHAT, but resulted in a higher specificity and positive predictive value in this population. Simultaneous testing requiring positive screening on both the ADOS and screening measure resulted in a higher positive

predictive value than when either respective screening measure was used alone. These results suggest further investigation into the use of a parent report measure, clinician follow-up, and structured observation of behavior to identify children in need of an autism specific evaluation.

**158.075 75** Convergence of Mullen Scales of Early Learning Developmental Quotient with the Differential Ability Scales, Second Edition Intelligence Quotient in Young Children. C. Farmer*[1], C. Golden[1] and A. Thurm[2], (1)*National Institute of Mental Health*, (2)*National Institutes of Health - National Institute of Mental Health*

Background:

Cognitive test selection is a recurrent challenge in autism spectrum disorder (ASD) research. Emphasis of common IQ tests on verbal ability, even on the so-called nonverbal testlets, can cause "floor" effects when standardized scores are not available for a given child's age range and raw score. Faced with these challenges, researchers often report the developmental quotient (DQ; mental age ÷ chronological age) in lieu of a standard score. Researchers also often choose to report only nonverbal DQ or IQ, with the understanding that these scores represent a more pure estimate of cognitive ability in individuals with ASD and significant verbal deficits. Due to these limitations in other tests, increasingly, the Mullen Scales of Early Learning (MSEL) and the Differential Ability Scales, Second Edition (DAS-II) have been used interchangeably, as both IQ and DQ, in cross-sectional and longitudinal analyses. Bishop et al. (2011) found that the MSEL had good convergent validity with the original DAS, but no data have been published on the relationship of the MSEL to the DAS-II, which has several notable changes from the first edition.

Objectives:

This study replicates and extends the Bishop et al. (2011) MSEL and DAS convergent validity analyses using the nonverbal (NV) and verbal (V) subscales of the MSEL and DAS-II in children with ASD and developmental delay (DD) versus typically developing (TD) children. Of primary interest was the MSEL DQ versus the DAS-II IQ, which is a relevant comparison for situations in which a child's chronological age exceeds his or her developmental level.

Methods:

Participants were drawn from a larger, longitudinal study of autism. Participants were 112 children aged 2 years to 9 years (M±SD=5.4±1.3), with a diagnosis of ASD or DD (n=70; 66% ASD) or TD (n=42). Mean scores in the TD group were DAS-II VIQ=113.9±11.7, DAS-II NVIQ=116.2±10.2, MSEL VDQ=105.9±10.8, MSEL NVDQ=106.0±11.8. Mean scores in the ASD+DD group were DAS-II VIQ=71.2±22.6, DAS-II NVIQ=77.9±20.2, MSEL VDQ=58.2±18.1, MSEL NVDQ=66.5±18.6.

Results:

MSEL NVDQ and DAS-II NVIQ were significantly ($p<.05$) correlated in both groups ($r_{ASD+DD}=.86$, $r_{TD}=.45$). However, the correlation between MSEL VDQ and DAS VIQ reached significance only in the ASD+DD group ($r_{ASD+DD}=.90$, $p<.001$; $r_{TD}=.30$, $p=.051$). For both nonverbal and verbal subscales, the interaction between group and MSEL in predicting DAS-II was significant, indicating that the relationships differed significantly between groups. Of further interest was the intercept in this model, which indicated that the DAS-II was an average of 20 points higher than the MSEL regardless of MSEL score. The groups did not differ significantly on the proportion with a MSEL/DAS difference of greater than one standard deviation for nonverbal ($n_{ASD+DD}=21$, 31%; $n_{TD}=14$, 33%) or verbal ($n_{ASD+DD}=33$, 48%; $n_{TD}=14$, 33%).

Conclusions:

This study finds support for the concurrent use of MSEL DQ and DAS-II IQ scores in ASD samples that span the range of cognitive and language abilities. However, caution is warranted when more cognitively able children are tested, especially using the verbal subscale, as the relationship between tests was much weaker when scores were higher.

**158.076 76** Exploring Gender Differences in Core Autism Symptoms. D. N. Lordo*, T. N. Takahashi and S. M. Kanne, *University of Missouri Thompson Center for Autism & Neurodevelopmental Disorders*

Background: Autism Spectrum Disorder (ASD) describes a range of complex neurodevelopmental disorders characterized by social and communicative impairments, as well as repetitive behaviors and/or restricted interests. Given that ASD is about five times more common in males

than females (Center for Disease Control and Prevention, 2013), and with evidence of a gender disparity in the clinical presentation of symptoms, many researchers have searched for male/female phenotypic differences. Few gender differences in ASD symptoms have been found in previous literature, and most findings have been related to IQ.

Objectives: To investigate the relationship between gender and core ASD symptoms in a large, well-characterized sample.

Methods: The study sample included 2,254 children and adolescents (1,957 males and 297 females) between the ages of 4 and 17 (M=9.0, SD=42.9), who participated in the Simons Simplex Collection, a multi-site genetic study focusing on simplex families. Logistic regression was used to examine whether specific variables concerning the core domains of communication, socialization, and repetitive behaviors were significantly related to gender using summary scores from the ADOS and ADI-R. Additionally, predictor variables included Vineland communication scores and ADOS module to measure functional language. Further regression analyses were then conducted to examine specific behaviors that may be predictive of gender (e.g., specific ADOS and ADI-R subscales).

Results: Significant predictors of core autism symptoms included IQ and repetitive behavior scores. No significant gender differences were found in the social and communication domains. There was a significant difference in IQ with males showing higher IQ than females. Further analysis of repetitive behaviors using ADI-R subscales showed males had significantly higher circumscribed interests and unusual preoccupations. In contrast, females had significantly more midline hand movements and an abnormal response to stimuli. Post hoc analyses indicated that only those individuals receiving ADOS Module 3 showed a significant difference in repetitive behaviors on the ADOS. Closer examination of Module 3 indicated that males showed a significant difference in a specific code related to greater interest in unusual or highly specific topics and repetitive behaviors.

Conclusions: Our study found a significant difference in aspects of behavioral phenotype between males and females. Consistent with past studies, IQ was significantly different with males having a higher average IQ than females. Additionally, repetitive behaviors, specifically circumscribed interests and unusual preoccupations, were more likely in males than females. Moreover, behaviors including midline hand movements and abnormal response to stimuli were more likely in females. These results suggest a gender discrepancy in the clinical presentation of core ASD symptoms.

**158.077 77** Sex Differences in Internalizing Symptoms in Young Children with ASD. N. B. Knoble*, S. W. Duvall, L. Huang-Storms, A. P. Hill and E. Fombonne, *Oregon Health & Science University*

Background: Few studies have examined sex differences in co-occurring behavioral and emotional problems among children with Autism Spectrum Disorder (ASD) and existing findings are mixed with some research suggesting increased affective symptoms in girls and externalizing symptoms in boys.

Objectives: To evaluate sex differences in co-occurring behavioral and emotional problems in a large clinical sample of children referred for and diagnosed with ASD.

Methods: 18 ATN sites, data collected from 2007 to 2013, on all subjects age 1.5 to 5.11 years with complete CBCL (version 1.5 to 5) and ADOS data (N=2941; mean age: 3.9 years, SD=1.08). Based on the T-scores, 5 narrow- and 3 broad-band CBCL scores were classified in 3 levels (Normal range: <60; Borderline: >=60 and <70; Clinical: >=70). CBCL data were also examined as continuous scores. Algorithm scores and calibrated severity ADOS scores were available as well as Vineland Adaptive Behavior Scales (VABS) on all participants.

Results: There were 2,446 boys (83.2%), 495 girls (16.8%), and no difference between sexes for mean age at assessment, ATN site, or ethnicity (Hispanic or not). There was a slight overrepresentation of girls among Black and "Other" race families (p=.05) and parents with higher education (p=.03).

No significant difference was found between sexes in levels of Somatic Complaints, Withdrawal, Attentional problems, Aggressive behaviors, Externalizing and Total CBCL scores (all p's>.15). Higher proportions of girls scored in the clinical

range for Anxiety problems (12.5% vs 7.7%; p=0.001) and Internalizing problems (32.3% vs 26.3%; p=.024). Similar results were obtained using continuous scores with girls scoring higher than boys on mean Anxiety T-scores and Internalizing T-scores (respectively: 57.8 vs 56.6, p=.01; 64.4 vs 63.1, p=.01); girls also showed higher scores on the Withdrawal scale (72.0 vs 70.9, p=.03) and on the Total score (64.8 vs 63.7, p=.04).

Further girls-only analyses on Anxiety and Internalizing scores indicated girls in the two older age groups (<3 y; 3 to 4.5 y; over 4.5 y) had slightly higher levels of anxiety, and significantly higher levels of Internalizing problems (chi-2=12.4, 4 df; p=.013). One-way ANOVAs (3 levels of anxiety: Normal, Borderline, Clinical) were used to compare means on 5 VABS standardized scores and 3 ADOS calibrated severity scores and yielded no significant difference for levels of Anxiety problems. In all VABS analyses, girls with Clinical levels of Internalizing problems scored lower (more impairment in Communication, Socialization, Daily Living Skills, Motor Skills and Adaptive Behavior Composite) than girls in the Normal range, with girls with Borderline levels scoring in-between the other 2 groups. For the ADOS calibrated severity scores, a trend was found for girls in the Normal range of Internalizing problems to have slightly less severe scores on the Repetitive and Restricted Behavior calibrated severity scale (p=.058).

Conclusions: Overall, findings suggest girls with ASD are more likely than boys to demonstrate anxiety and internalizing problem behaviors; however, there were no sex differences found in regards to externalizing problem behaviors. Follow-up analyses will examine affective and behavioral differences by gender among older children with ASD.

**158.078 78** Utility of the Child Behavior Checklist in Differentiating Children with Autism Spectrum Disorders from Other Clinical Disorders. A. Havdahl*[1], S. L. Bishop[1], M. Huerta[2] and E. Molloy[1], (1)*Center for Autism and the Developing Brain, Weill Cornell Medical College*, (2)*Weill Cornell Medical College*

**Background:**

Identification of ASD is often challenging due to the heterogeneous presentation and symptom overlap with other clinical disorders (OD). "Best practice" diagnostic assessment of ASD is time- and resource-intensive, due to the need for in-depth assessment of functioning and behavior with autism-specific instruments by clinicians with specialized training (Huerta & Lord,2012). Thus, there is a pressing need for screening tools to identify children most in need of further ASD-specific assessment.

Recent reports have suggested that the CBCL (Achenbach & Rescorla,2001) may be useful in screening for ASD.

Three CBCL profiles in particular have been found to differentiate ASD from OD, including the Withdrawn (WD) subscale in both age versions, the Pervasive Developmental Problem(PDP) in the preschool version, and the "CBCL-ASD-Profile"(CAP) consisting of subscales WD, Social problems and Thought problems in the school version (Biederman et al.,2010;Narzisi et al.,2013,e.g.). However, studies examining their predictive validity have been limited by small samples of children with ASD, and comparison groups that have excluded children with cognitive impairments. Additionally, diagnostic accuracy may vary by gender and IQ level (Sikora et al.,2008).

Due to widespread use of the CBCL as a routine screening instrument in mental health settings worldwide, reports of its usefulness in screening for ASD may lead clinicians to choose this over autism-specific screening tools. Thus, further study of its ability to correctly identify children with ASD is clearly warranted.

**Objectives:**

Examine the utility of proposed CBCL profiles for ASD in differentiating children with ASD from OD, and potential differences by gender and nonverbal IQ (NVIQ).

**Methods:**

Participants were 226 children with ASD and 174 children with OD (mainly ADHD/ODD, Anxiety/Mood disorder, and Intellectual Disability;ID), recruited as part of a research study. Diagnoses were made based on information from comprehensive assessments for ASD including questionnaires, ADI-R, Vineland-II, ADOS and cognitive testing.

Diagnostic accuracy for ASDdiagnosis was analyzed using ROC-analyses and area under the curve (AUC) scores. Analyses were done for the whole sample, and by gender and NVIQ (above/below 70). T-scores were used for WD and PDP, and the sum of raw scores of WD, Thought Problems and Social Problems for CAP.

**Results:**

Overall, the diagnostic accuracy for ASD was poor, with AUC at .67 for WD-preschool-aged, .66 for WD-school-aged, .67 for PDP, and .68 for CAP. At cutoffs low enough to obtain sensitivities at 80% (80-85%), specificities were low (38-48%).

Girls had better AUC-scores for PDP (.83 vs .61), WD-preschool-aged (.80 vs .63), and CAP (.72 vs .67), but not for WD-school-aged (.65 vs .67). For PDP, a cutoff of 61 correctly classified 95% of girls and 77% of boys with ASD, and 61% of girls and 44% of boys with OD.

ROC-analyses by NVIQ only showed better than poor AUC for CAP, which was moderate for higher IQs, but very poor for low IQs.

**Conclusions:**

The CBCL has limited utility in differentiating between children with ASD and OD such as ADHD/ODD, anxiety/mood disorders and ID. Our results do not support its use in place of well-established screening tools for ASD.

**158.079 79** Assessing Verbal Ability in Children with ASD: Convergent Validity of the Ppvt-IV. S. Maisel[1], F. I. Jackson*[1], E. Hanson[1] and A. V. Snow[2], (1)*Boston Children's Hospital*, (2)*Boston Children's Hospital, Harvard Medical School*

Background: The Peabody Picture Vocabulary Test-IV (PPVT-IV; Dunn & Dunn, 2007) is a one-word receptive vocabulary assessment. Recent studies of individuals with Autism Spectrum Disorder (ASD) have used PPVT-IV scores as estimates of verbal or cognitive ability (e.g., Peterson et al., 2013; ). To date, the extent to which PPVT-IV scores represent a valid estimate of overall verbal or cognitive ability in individuals with ASD has not been examined.

Objectives: The current study examined the convergent validity between the PPVT-IV and standardized cognitive assessments (Mullen Scales of Early Learning (Mullen) and Diagnostic Ability Scales (Early Years (DAS EY) and School Age Forms (DAS SA)). Subject characteristics influencing the relationship between cognitive assessment scores and PPVT-IV scores were also examined.

Methods: Participants included 2643 (86.7% male) children between 47-211 months (mean = 82.5, SD = 31.5) who participated in the Simons Simplex Collection. Age equivalents of full-scale IQ (FSIQ) and verbal IQ (VIQ) scores on the Mullen and DAS were correlated with PPVT-IV age equivalents using Pearson's correlations. The effect of subject characteristics (age, gender, ADOS CSS score, and FSIQ) on the relationship between the PPVT-IV and VIQ was examined using Linear Mixed-Effects Models.

Results: High positive correlations were found between the PPVT-IV and the full scale and verbal age equivalents of the Mullen ($r = 0.83$ and $r = 0.82$ respectively). Analyses also indicated high correlations between the PPVT-IV and the Mullen receptive and expressive verbal subscale age equivalents ($r = .80$ and $r = .74$). Age was associated with differences between the PPVT-IV and Mullen verbal IQ ($p < 0.05$), such that PPVT and VIQ scores were more similar in younger participants.

For the DAS EY, results indicated moderate and high positive correlations between the PPVT-IV and FSIQ and VIQ scores ($r = 0.59$ and $r = 0.76$, respectively). FS IQ was a significant predictor of the difference between PPVT-IV and VIQ Z scores ($p = 0.002$), such that children with lower FSIQ scores had a smaller difference between PPVT-IV and VIQ scores.

For the DAS SA, results indicated moderate and high positive correlations between the PPVT-IV and DAS SA FSIQ and VIQ scores ($r = .79$ and $r = .87$, respectively). FSIQ, ADOS CSS, and gender were significant predictors of differences in the PPVT-IV and the DAS School Age VIQ Z scores ($p < 0.001$).

Conclusions: Results indicated moderate and high positive correlations between FSIQ and VIQ scores and PPVT-IV scores, indicating a strong relationship between PPVT-IV scores and estimates of verbal and cognitive ability. The agreement between PPVT-IV and VIQ scores is affected primarily by level of functioning. This indicates that the PPVT-IV is a better estimate of

overall verbal ability in lower functioning children with ASD. Researchers and clinicians who use the PPVT-IV to estimate overall verbal functioning should be aware that this practice is most valid for lower functioning children with ASD.

**158.080 80** Developmental Stability of Sensory Processing Patterns in Autism, Attention Deficit Hyperactivity Disorder and Typical Development. L. M. Little*, E. Dean, L. Foster and W. Dunn, *University of Kansas Medical Center*

Background: Sensory features, which cluster into sensory processing patterns, differ among diagnostic groups (e.g., Baranek et al., 2006; Dunn & Bennett, 2002). There is limited evidence, however, related to the developmental correlates of sensory processing patterns across diagnostic groups, particularly related to autism spectrum disorders (ASD) and Attention Deficit Hyperactivity Disorder (ADHD). Using normative data from the forthcoming Children's Sensory Profile 2nd Edition (Dunn, in preparation), we examined sensory processing patterns (i.e., sensitivity, avoiding, registration, seeking) among children with ASD, ADHD, and typical development (TD).

Objectives: (1) Determine the extent to which sensory processing patterns (i.e., sensitivity, avoiding, registration, seeking) differ across children with ASD, ADHD, and typical development; and (2) Investigate the effect of chronological age on the association between diagnostic group and sensory processing patterns.

Methods: This cross sectional study used data from the Sensory Profile 2nd Edition (Dunn, in preparation). Participants included children ages 3-14 years with a diagnosis of ADHD (N=53; mean age=8.8 yrs; SD=2.76 yrs), ASD (N=61; mean age=7.50 yrs; SD =2.76 yrs), and TD (N=56, mean age=8.09 yrs; SD =2.80 yrs). We used multivariate analysis of covariance (MANCOVA) to examine the extent to which the differences in sensory processing patterns among diagnostic groups were moderated by chronological age.

Results: Findings from the MANCOVA suggest that diagnostic groups significantly differ on sensory processing patterns, Pillai's Trace [$F(2,143)=606.8$, $p<.001$]. Post-hoc LSD tests revealed significant differences between TD, ASD, and ADHD groups on each sensory processing pattern (each $p<.01$). ASD and ADHD significantly differed on avoiding ($p<.05$); ASD demonstrated increased avoiding. Chronological age was not a significant variable in explaining the association between diagnosis and sensory response pattern.

Conclusions: Findings from this study suggest that the differences in sensory responses persist throughout childhood and into adolescence for individuals with ASD and ADHD as compared to those with TD. Although previous studies show that registration differences differentiate children with ASD at younger ages (e.g., Ben-Sasson et al., 2009), our results suggest that children ages 3-14 years with ASD demonstrated significantly more avoiding. As children with ASD get older, they have more specificity about what sensory experiences are acceptable. Sensory response patterns remained relatively stable for individuals across diagnostic groups, suggesting that intervention approaches that focus on making adaptations may be more effective than altering individual children's responses to sensory stimuli.

**158.081 81** Differences in Parent Reported Adaptive and Executive Functioning Between African American and White Children with ASD. A. B. Ratto*[1], L. Kenworthy[2], A. C. Armour[2], K. M. Dudley[2], Y. Granader[2] and L. G. Anthony[2], (1)*Children's National Health System*, (2)*Children's National Medical Center*

Background: Research into cultural differences in the symptom profile of autism spectrum disorder (ASD) is limited. However, prior studies have reported that children from ethnic minority backgrounds display greater impairments in several areas, including social symptoms, language, cognition, and motor skills (Cuccaro et al., 2007; Tek & Landa, 2012). Prior studies have utilized early childhood samples, including children with developmental delays. Further research is needed to investigate ethnic differences in symptoms, particularly in older and higher-functioning samples.

Objectives: The goal of the present study was to examine differences between African American (AA) and White children with ASD in parent-reported adaptive behavior and executive function. Based on prior research, it was hypothesized that AA children would have greater impairments in both domains.

Methods: Participants included children with a confirmed diagnosis of ASD, ages 5-18 years with an IQ>70, recruited as part of a larger research

study and through clinical evaluation. From the initial sample of 966 participants, the final sample of AA (n=38) and White (n=233) participants with complete data was generated. There were no significant differences between the groups on age, gender, diagnosis of ADHD, or ADHD medication use; however, AA participants had significantly lower IQ scores (t=3.28, p<.01). Parent report on the Behavior Rating Inventory of Executive Function (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000) and the Vineland Adaptive Behavior Scales-II (Sparrow, Cichetti, & Balla, 2005) was compared across the AA and White groups.

Results: On the BRIEF, White children showed significantly greater impairment on the Global Executive Composite (GEC; t=2.09, p<.05) and the Behavior Regulation Index (BRI; t=2.37, p<.05), and greater impairment approaching significance on the Metacognitive Index (MCI) of the BRIEF (t=1.84, p<.10). Hierarchical multiple linear regression analyses indicated that ethnicity was no longer a significant predictor of BRIEF scores after controlling for IQ, gender, ADHD diagnosis, and medication use. The results of stepwise regression analyses entering all variables into the model and statistically selecting the model that accounted for the greatest proportion of variance indicated that gender best predicted both GEC (F= 5.78, p<.01) and MCI (F=6.36, p<.05) scores, while a model using both gender and ethnicity best predicted BRI scores (F=4.06, p<.05).

No significant group differences were observed in Vineland scores. Stepwise regression analyses indicated that IQ scores best predicted Vineland total scores in the overall sample (F=17.69, p<.001) and within the White sample (F=17.76, p<.001), with a small effect size ($R^2$=.08, both samples). Within the AA sample, IQ did not significantly predict Vineland total scores, likely due to reduced power within the AA sample, but did significantly predict communication scores (F=8.56, p<.01).

Conclusions: The results suggest a mixed profile of ethnic differences. Although ethnic differences were observed on the BRIEF, these were better accounted for by other factors. In contrast to prior studies, no differences were found on in adaptive behavior. The present study's use of an older sample without intellectual disability may suggest that ethnic differences in prior research are best explained by higher rates of developmental delay in ethnic minority children with ASD.

**158.083 83** Factors Associated with Parents' Ratings of the Severity of Autism Spectrum Disorder: A Population Study. B. Zablotsky*, S. J. Blumberg and M. D. Bramlett, *National Center for Health Statistics*

**Background**: There is currently little consensus on how severity of a child's autism spectrum disorder (ASD) should be measured (Bernier, 2012). Definitions of severity have been based on criteria such as the number and intensity of core symptoms, the child's overall level of functional impairment, and the child's ASD diagnosis subtype (e.g. Asperger's Disorder, Autistic Disorder). Additional definitions have focused on the presence of secondary diagnoses, including intellectual disabilities, behavioral problems and learning disabilities. Despite this lack of a standardized definition, parents are readily able to answer a question asking them to describe the severity of their child's ASD. The goal of the current study is to examine the basis for a parent's judgment of ASD severity.

**Objectives**: Identify child and family factors that are associated with a parent's severity rating of their child's ASD.

**Methods**: Data come from two national surveys, the 2009-2010 National Survey of Children with Special Health Care Needs (NS-CSHCN) and a follow up survey to the NS-CSHCN, the 2011 Survey of Pathways to Diagnosis and Services ("Pathways"). Parents in households with a child diagnosed with an ASD between the ages of 6-17 were eligible for the current study. To be included in the final sample the parent had to have completed both surveys, including a mailed module in the Pathways survey (*n*=967). Parents answered questions about the severity of their child's ASD (mild, moderate or severe), autism symptoms (utilizing the Children's Social Behavioral Questionnaire (Hartman, 2006)), the impact of the child's condition on the family, and the impact of the child's condition on the child's social and behavioral health (utilizing the Strengths and Difficulties Questionnaire (Goodman, 1997)). A survey weighted measurement model was created utilizing Mplus software to generate latent factors of child impact, family impact and child symptoms. Additional analyses were completed in Stata 12.0.

Associations between demographic characteristics and level of parent-reported severity were calculated utilizing weighted $\chi^2$ tests. Separate weighted multivariate logistic regression models, adjusted for demographics of the child and family were fitted to compare different severity groups by latent factors.

**Results:** Chi-square tests revealed that children with a mild severity rating were younger than children with a moderate or severe severity rating. Children with a mild ASD were less likely to have anxiety, depression, behavioral and conduct problems or an intellectual disability when compared to children with more severe ASD. In adjusted models, children with moderate ASD had more severe symptoms (OR=2.16, 95% CI:1.38-3.41, *p*=.001) and family impacts (OR=1.79, 95% CI:1.26-2.54, *p*=.001) than children with mild ASD. Meanwhile, children with severe ASD had higher family impacts (OR=2.80, 95% CI:1.66-4.72, *p*<.001) than children with moderate ASD, but not higher symptoms.

**Conclusions:** A parent's conceptualization of their child's ASD may primarily vary as a function of the impact of the child's disability on the family, and to a lesser extent on the impact the child's disability has on the child. Therefore, a parent's conceptualization of severity may not always coincide with objective or clinical assessments focused on symptoms or functional impairment (Perrin et al., 1989).

**158.084 84** How Will DSM-5 Affect Autism Diagnosis? a Systematic Literature Review and Meta-Analysis. K. M. Kulage*, A. M. Smaldone and E. G. Cohn, *Columbia University*

Background: The prevalence of autism spectrum disorders has steadily increased over the past decade, leading to the emergence of autism as a major public health concern. In May 2013, the American Psychiatric Association published the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) which revised DSM-IV-TR autism subgroups of autistic disorder (AD), Asperger's Disorder, and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) to combine them into one broad diagnosis—autism spectrum disorder (ASD). The new ASD definition now includes only two main behavior categories, social communication and interaction and restrictive, repetitive behaviors.

Objectives: Because the new DSM-5 criteria for ASD has the potential to affect the number of children and adults who currently have or may become eligible for access to care and insurance coverage for ASD, we conducted a systematic review and meta-analysis to (1) estimate the changes in frequency of ASD diagnosis based on the proposed DSM-5 criteria; (2) determine the ASD subgroups most likely to be affected by the changes in DSM-5 criteria; and (3) present public health policy implications of implementation of DSM-5 ASD criteria.

Methods: Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we searched the literature for studies that applied both DSM-IV-TR and DSM-5 autism diagnosis criteria to study samples. Three reviewers rated the scientific rigor of each study using the Quality Appraisal of Reliability Studies (QAREL), an 11-item checklist. Data were extracted as sample size, subjects meeting DSM-IV-TR criteria, and number no longer meeting ASD diagnostic criteria under DSM-5. Pooled effects were estimated for the proportion of subjects who no longer met criteria for ASD diagnosis and for subgroups (AD, Asperger's Disorder, PDD-NOS) using random effects meta-analysis models. The heterogeneity of each model was assessed using Cochran Q and $I^2$statistics. Publication bias was examined using a funnel plot.

Results: Of 418 studies identified by the search, 14 met inclusion criteria for the systematic review and meta-analysis and 7 studies specifically examined DSM-IV-TR subgroups (AD n=7; Asperger's Disorder n=4; PDD-NOS n=6). The most consistent area of weakness in study quality was lack of blinding with only one study reporting that raters were blinded to the results of DSM-IV-TR. All studies consistently reported decreases in ASD diagnosis (range 7.3-68.4%) and the DSM-IV-TR subgroups of Asperger's Disorder (16.6-100%) and PDD-NOS (50-97.5%) using DSM-5 criteria. There were statistically significant pooled decreases in diagnoses for ASD (31% [95%CI 20.4-44.3], p=0.006) and the DSM-IV-TR subgroups of AD (22% [95%CI 16-29], p<0.001) and PDD-NOS (70% [95%CI 55-82], p=0.01); however, the pooled decrease for Asperger's Disorder was not significant (70% [95%CI 26-94], p=0.38). Significant heterogeneity was present in all models. There was no evidence of publication bias.

Conclusions: DSM-5 will likely decrease the number of individuals diagnosed with ASD, particularly the DSM-IV-TR PDD-NOS subgroup. Future research is needed to examine implementation of DSM-5 on diagnosis of autism and how states respond regarding insurance coverage and services for individuals without an ASD diagnosis but who still may require assistance.

**158.085 85** Measures of Symptom Severity in Preschoolers with Autism Spectrum Disorder: The Role of Maternal Anxiety. C. S. Ghilain*[1], M. V. Parladé[1], T. D. Owen[1], C. Alvarez-Tabio[1], A. Gutierrez[2] and M. Alessandri[1], (1)*University of Miami*, (2)*Florida International University*

Background: Approximately 38% of first-degree relatives of children with Autism Spectrum Disorder (ASD) are diagnosed with an anxiety disorder (Smalley, et al., 1995). Mothers of very young children recently diagnosed with ASD report significantly increased psychological distress as measured by mean scores on anxiety and depression scales, even when compared to mothers of children with other developmental disabilities (DD; Estes, et al., 2009). Additionally, previous research suggests that parents who have been diagnosed with an Axis I Disorder (e.g., mood or anxiety disorders) may over report the severity of ASD symptoms in their children (Winterrowd, et al., 2008).

Objectives: This research examined the relationship between maternal anxiety and parent-report and objective measures of ASD symptom severity. Specifically, it was hypothesized that parent-reported symptoms of ASD would not be significantly correlated with clinical symptom severity. Additionally, maternal anxiety and clinical assessment of ASD severity was not expected to be significantly correlated; however a positive and significant relationship between maternal anxiety and parent-reported symptom severity was expected.

Methods: The sample consisted of 198 preschool-aged children with ASD (82% male) who were followed throughout the school year as part of a completed multi-site study comparing comprehensive treatment models (Boyd, et al., 2013). Children were between the ages of 3 and 5 years during enrollment (*M* = 48 mo. *Range* = 34-62 mo.), and were evaluated at three time points (pre-test, post-test, and follow-up). Only data collected at pre-test were utilized in the current study. The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999) was used to measure clinical assessments of symptom severity. ADOS severity scores were then compared to parent-reports of symptom severity, as measured by the Social Responsiveness Scale (SRS; Constantino, 2003). The relationship of each measure to self-reported maternal anxiety scores on the Endler Multidimensional Anxiety Scales – Trait (EMAS-T) was also assessed (Endler, et al., 1991).

Results: Pearson *r*s were calculated to determine the correlation between maternity anxiety scores on the EMAS-T, and symptom severity scores on the ADOS and SRS. No significant relationship was found between clinical symptom severity and parent-reported symptom severity ($r(182) = .072$, $p = .331$). Further, standardized clinical symptom severity and maternal anxiety were not significantly related ($r(180) = .050$, $p = .509$). However, a strong relationship between parent-reported symptom severity and maternal anxiety level was detected ($r(182) = .269$, $p = .001$). Results provide support for our hypotheses and indicate that parent-reported symptom severity scores are not significantly related to objective measures of symptom severity; however, a significant relationship does exist between maternal anxiety and parent-reported symptom severity.

Conclusions: Results indicate that parents and clinicians may not agree on ASD symptom severity and suggest the possibility that maternal anxiety may be an influential factor. The potential implications of a relationship between maternal anxiety and parent perception of symptom severity are discussed. Future studies may investigate the impact of maternal anxiety on diagnostic decisions and/or parent-child relationships, with the ultimate goal of improving quality of life for family members impacted by ASD diagnosis.

**158.086 86** Measuring Joint Attention in Children with Autism Spectrum Disorder through Structured and Unstructured Play. J. Panganiban*[1] and C. Kasari[2], (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

Background: Joint attention, or the shared experience of an object or activity, is one of the earliest indicators of social interaction, and an important precursor to language. Skills used to coordinate joint attention often emerge within the

first and second years of life. Research shows that children with an autism spectrum disorder (ASD) exhibit atypical development of joint attention skills compared to typically developing children. Considering the important role joint attention plays in language development, the accurate assessment of joint attention skills in children with ASD is critical for identifying deficits and designing early interventions. The commonly accepted gold standard for joint attention assessment is the Early Social Communication Scales (ESCS). However, researchers and clinicians may benefit from expanding their methods of joint attention assessment. Multiple observations across different constructs may improve the accuracy of assessing a child's development of joint attention, and improve ecological validity.

Objectives: The current study aims to explore the validity of measuring joint attention within structured and unstructured play interactions by comparing rates of joint attention in these contexts with rates of joint attention in the ESCS.

Methods: Using the same guidelines established by the ESCS, joint attention skills were coded from structured play assessments and unstructured caregiver child interactions administered to 28 young children with ASD, ages 2 to 5 years.

Results: Correlation analysis shows strong positive correlations between rates of child initiated joint attention in structured ($r(26) = .67$, $p < .01$) and unstructured ($r(26) = .61$, $p < .01$) play when compared to the ESCS. Comparison of correlation coefficient rates in a multitrait-multimethod matrix provides evidence of convergent and discriminant validity for measuring joint attention skills during structured and unstructured play.

Conclusions: These findings suggest that structured and unstructured play assessments can be utilized as tools to measure child initiated joint attention in children with ASD. By gathering information from a variety of assessment contexts, researchers and clinicians can be more confident in their assessment of these skills. Furthermore, being able to validly assess joint attention in unstructured settings can provide researchers and clinicians more flexibility when working with highly impacted or very young individuals. Overall, these findings provide evidence for an increase in efforts to include more ecologically valid methods of measurement among individuals with ASD.

**158.087 87** Microanalysis of Daily Living Skills in Adolescents with ASD. A. W. Duncan*[1], M. Will[1], K. Martin[1], H. Barnard[1], C. L. Thomas[2] and R. E. Adams[1], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Cincinnati Children's Hospital*

Background: The acquisition and mastery of daily living skills is critical for achieving certain milestones in adulthood including living independently, attending post-secondary education, maintaining a job, and socializing with others. Adolescents with autism spectrum disorder (ASD) have daily living skills that are significantly impaired and fall far below what would be expected based on both their chronological age and cognitive abilities (Duncan & Bishop, in press; Klin et al., 2007). Despite these impairments, there has been a dearth of research on interventions that target the acquisition and maintenance of essential daily living skills that may then facilitate or lead to a more successful adult outcome for individuals with ASD. However, before effective interventions can be developed, it is critical to understand what specific skills or skill sets are impaired in adolescents with ASD.

Objectives: The current study's primary aim was to examine the specific strengths and difficulties of adolescents with ASD in the 3 Daily Living Skills subdomains of the Vineland Adaptive Behavior Scales, 2$^{nd}$Edition (Vineland-II) by analyzing specific items and content categories.

Methods: Seventy-five parents of adolescents with ASD completed the Vineland-II as part of a larger study investigating issues related to the transition to adulthood. Adolescents with ASD ranged in age from 12-17 years (M = 181.9 months). Over 75% of diagnoses of ASD were confirmed by cross referencing the adolescent's electronic medical record. Both individual items and content categories (e.g., Telephone Skills, Money Skills) for the 3 Daily Living Skills subdomains (i.e., Personal, Domestic, and Community) of the Vineland-II were examined for the current study. A score was calculated for each content category that indicated the percentage of possible points earned within each category.

Results: Data collection and analysis is ongoing and the sample is expected to exceed 100

participants by May 2014. Adolescents were predominately male (92%) and Non-Hispanic (98.7%). Preliminary analyses indicated the following: (1) Participants had mean scores on the 3 Vineland-II domains that fell within the Adequate range and had mean age equivalent scores that ranged from 9 to 11 years of age; (2) Adolescents with ASD were proficient in the content domains of Eating and Drinking (mean score of 93.9%), Toileting (mean score of 87.6%), Dressing (mean score of 86.1%), and Time and Dates (mean score of 82.6%); (3) Adolescents with ASD had particular difficulties in the areas of Healthcare (mean score of 45.5%), Housekeeping (mean score of 32.6%), Job Skills (mean score of 22.3%), and Going Places Independently (mean score of 14.8%). Additional analyses will be conducted to further explore specific items and examine relationships between socio-demographic factors and daily living skills.

Conclusions: The preliminary results indicate that adolescents with ASD appear to have daily living skills deficits that will likely affect their ability to achieve a successful adult outcome. Future research and implications for interventions that focus on current functioning and future adult outcomes by increasing skills that are needed for independent living, employment, post-secondary education, and socialization with peers in adolescents with ASD will be discussed.

**158.088 88** Motors Skills in High Functioning Autism. C. Gallot*[1], A. Amestoy[1], E. Bestaven[2], E. Guillaud[2], J. R. Cazalets[2] and M. Bouvard[3], (1)*Centre Ressource Autisme Aquitaine*, (2)*INCIA - CNRS UMR 5287*, (3)*Expert Autism Center*

Background: High Functioning Autism (HFA) is part of Autism Spectrum Disorder (ASD). It is characterized by impairment in social interaction and repetitive behaviour but without intellectual disability. Clinically, by six months of age they present with motor impairments and then 50% of them present Developmental Coordination Disorder (DCD), with major impacts on social and working life. By contrast, there are few studies on motor skills in ASD, and their results are heterogeneous.

Objectives: The objectives of this study are: (1) to describe motor skills in HFA, using objective movement analyzing tools, on different motor levels from the reflex and automatic level (« low level »), to the voluntary level (« high level »); (2) to evaluate the cognitive demand of motricity. Our hypotheses are: (1) Subjects with HFA present with impairment in low and high level movements. (2) They have an impairment in dual task (motor and cognitive task) compared to typically developing subjects**.**

Methods: Motor functioning has been first evaluated clinically with a validated standardized scale of motor development (DCDQ) and a medical interview based on DCD's DSM 5 criteria. We evaluated motor skills in a movement laboratory (using posturography, kinematic analysis and pointing monitoring) during four motor tasks (standing, walking, pointing and intercepting task) and during three dual tasks (walking with alphabet, talk and counting). We included twenty-eight participants aged of 12 to 30 years old: 14 subjects with HFA and 14 typically developed subjects.

Results: Clinically, half of the participants with HFA presented with impairment in motor functioning, and with alteration of childhood motor development. These results are consistent with DCD prevalence in ASD (50%). Experimentally, we found a tendency in impairment of low level motor ability (standing and walking eyes opened) and a significant alteration in the high level motor skills (pointing and interception) associated with an impairment in complex motor integration (dual task and standing with eyes closed).

Conclusions: In this study, we showed that HFA individuals are capable of performing a range of motor skills, but that they are perhaps using modified processes: overweighted vision, slower motor planning while accuracy is intact, high cognitive requirement of motricity, more variable movements. Furthermore, HFA individuals present major impairments in different areas of functioning. Automatized tools seem to be interesting to develop early screening tools and potential biomarker.

**158.089 89** Sensory-Motor Control in Autism. C. Whyatt*, *Queen's University Belfast*

Background:

Despite being typically characterized as a social deficit, research has repeatedly highlighted the presence of measurable motor problems associated with Autism Spectrum Disorders (ASD) (Fournier et al, 2010). In particular, performance

comparisons imply distinct difficulties in the areas of *manual dexterity and ball skills* (e.g. Green et al., 2010; Whyatt & Craig, 2012). However, the nature and thus potential root of these difficulties remains unclear.

Objectives:

This research aimed to further profile motor control in children diagnosed with ASD. Specifically, levels of spatial and temporal control were assessed during a manual dexterity task, measuring the ability for participants to use external sensory information to prospectively control and guide action. Moreover, we aimed to provide insight into underlying cognitive-motor interaction, by using two distinctive control groups, independently matched for verbal and non-verbal IQ. These refined comparisons allowed problems *specific* to autism to be identified.

Methods:

Building on preliminary assessment using the Movement Assessment Battery for Children (Whyatt & Craig, 2012), this study explicitly assessed levels of performance on a controlled manual dexterity trace task. Participants were asked to successfully 'draw' through a maze presented on a touch screen tablet. Three levels of task difficulty were presented, allowing in-depth assessment of underlying spatial and temporal control. Comparisons of performance were made between children diagnosed with ASD (aged 9-11) and two distinct, age-matched control groups.

Results:

Preliminary assessment of spatial performance implied a significant impairment in the ASD group in relation to both the non-verbal ($p<.05$) and receptive language ($p<.05$) control groups. Kinematic assessment revealed similarities between the ASD and receptive language group, with specific difficulties tailoring temporal characteristics of the movement to maximize spatial accuracy. However, more complex levels of precise temporal control, including the use of corrective sub movements and deceleration into corner sections of the maze, successfully differentiated between the ASD and *both* control groups ($p<.05$).

Conclusions:

This study has demonstrated that poor levels of manual dexterity in ASD are potentially due to fundamental problems with perception-action coupling leading to difficulties with both prospective and online control. Moreover, results demonstrated similarities between children diagnosed with ASD and typically developing children matched on age and receptive language, highlighting the importance of independently controlling for facets of IQ.

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Green, D., Charman, T., Pickles, A., Chandler, S., Loucas, T., Simonoff, E., & Baird, G. (2010). Impairment in movement skills of children with autistic spectrum disorder. *Developmental Medicine and Child Neurology*, *51,*311-316.

Whyatt, C. & Craig, C.M. (2012). Motor Skills in Children aged 7-10 years, diagnosed with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, *42(9)*, 1799-1809.

**158.090 90** Temporal Aspects of Gait in Autism. K. R. Forster[1], B. Nicholas*[1] and D. C. Wimpory[2], (1)*Bangor University*, (2)*Bangor University & BCU Health Board*

Background:

Atypical gait is often seen in children with Autism Spectrun Disorders (ASD), although there are incosistencies of results with regards to how specific gait parameters associate with ASD. The idea that gait analysis might be useful in diagnosis of ASD is therefore currently debatable. Different methods of measurent of multiple aspects of gait, at different sensitivities across studies may account for some of these inconsistencies. This study investigates exclusively high resolution temporal measures of gait in ASD.

Objectives:

To compare temporal aspects of gait in typically developing individuals and those with ASD. To obtain high resolution, exclusively temporal measurements of gait for the two sample groups. To consider possible diagnostic value of the findings.

Methods:

Using Vicon MX and 12 MXF40 motion capture systems sampling at 250Hz, Duration of step, stance and swing were assessed in 16 participants with High Functioning Autistic Spectrum Disorders (ASDs) (7-35yr), and 16 age matched Typically Developing (TD) controls. Participants performed multiple straight-ahead walks, aimed to capture seven strides suitable for data analysis. Strides were selected mid-walk, once walking rhythm was established and before deceleration. Mean and coefficient of variation(CoV) for each gait parameter was calculated.

Results:

No significant difference was found between the ASD and TD groups in terms of the average stride, stance or swing duration. However, analysis of CoV values showed a significant difference in temporal variability of step, stance and swing between the 2 groups ($p<0.001$), with the HFA group having higher CoV for each parameter. There was also significant difference in left vs right foot variability of these measures for the HFA group compared to TD controls.

Conclusions:

The results of this investigation suggest temporal analysis of aspects of gait as a possible biometric in ASD research and diagnosis.

**158.091 91** The Effects of Birth Order and Birth Spacing on Autism Symptom Severity in Simplex Families. N. Roberts* and L. Martin, *Azusa Pacific University*

**Background:**

Previous research has demonstrated several interesting findings related to birth order and birth spacing and autism spectrum disorder (ASD). Regarding birth order, studies have found an increase in the severity of ASD between first and second born siblings. Other studies have reported an increased incidence of ASD in second born children compared to first born children. The increases in severity and incidence appear to be related to the spacing between pregnancies. To further explore this phenomenon, we looked at measures of ASD severity across birth orders in the Simons Simplex-Collection (SSC) dataset, created by the Simons Foundation Autism Research Initiative (SFARI).

**Objectives:**

The purpose of this study is to analyze how birth order and birth spacing affects autism symptom severity. To this end, comparisons were made between first and second born ASD cases. In addition, ASD cases that were born within 2 years of an older sibling were compared to those that were born greater than 2 years after a sibling.

**Methods:**

The SSC collection consists of data collected from 12 participating university-affiliated research clinical sites. The data is a comprehensive collection of approximately 4,000 to 6,000 phenotypic data points for each SSC family. As a starting point, we compared data from several measures including: Social Responsiveness Scale (SRS), Vineland Adaptive Behavior Scale-II (VABS-II), Child Behavior Checklist (CBCL), and verbal and non-verbal intelligence scores. Independent samples t-tests using Bonferroni corrected alpha levels were used to determine significant differences in clinical measures of ASD severity.

**Results:**

The group of second born ASD cases demonstrated significantly greater symptom severity than the group of first born ASD cases across multiple measures. Furthermore, the group of ASD cases born within 2 years of an older sibling was shown to exhibit significantly greater symptom severity than the group of ASD cases born more than 2 years after a sibling. This finding was also observed across multiple measures.

**Conclusions:**

The results of this study confirm and extend previous studies on the effects of birth order and birth spacing on ASD. ASD symptoms were more severe in probands who were born after an unaffected sibling, especially if their birth occurred within 2 years of their older sibling.

**158.092 92** Validation of the Parent-Report and Teacher-Report Social Responsiveness Scale (SRS) in the Netherlands. J. Duvekot*[1] and K. Greaves-Lord[2], (1)*Erasmus MC-Sophia Children's Hospital*, (2)*Yulius*

Background: The Social Responsiveness Scale (SRS) is a widely used Autism Spectrum Disorder

(ASD) questionnaire that can be completed by parents and teachers. In several countries, the SRS has been found to be able to discriminate between children with ASD and children with other psychiatric disorders. However, the validity of the Dutch version of the SRS in a high-risk sample remains to be investigated. In addition, few studies have investigated the validity of the teacher-report SRS.

Objectives: The aims of the present study were to investigate 1) agreement between the parent-report and teacher-report SRS scores and 2) correspondence of the parent-report and teacher-report SRS scores to ASD classifications on standardised diagnostic instruments: the Autism Diagnostic Observation Schedule (ADOS) and the Developmental, Dimensional and Diagnostic Interview (3Di).

Methods: Our sample consisted of 283 children aged 4-10 years who had been referred to one of six mental health care centres in the Netherlands. For each consecutive referral, both a parent and a teacher were asked to complete the SRS. For research purposes, children with a positive screen on the parent-report SRS (total raw score ≥75, $n$ = 390) and a random selection of children with a negative screen ($n$ = 202) were invited for in-depth diagnostic assessments including the ADOS and the 3Di. Of these, 203 screen positives and 80 screen negatives participated in at least one diagnostic assessment. For $n$ = 255 (90%) we also had a completed teacher-report SRS. Pearson correlation was used to investigate parent-teacher agreement on the SRS. Receiver Operating Characteristic (ROC) analyses were used to examine the ability of the parent-report and teacher-report SRS to predict ASD classifications on either the ADOS or the 3Di or on both.

Results: In the total sample of $n$ = 283, 43% (109 out of 251) of the children were classified as having ASD on the ADOS, 48% (115 out of 241) on the 3Di and 26% (55 out of 209) on the ADOS as well as the 3Di. The correlation between the parent-report and teacher-report SRS scores was $r$ = .28 ($p$ < .01). For the parent-report SRS the Area Under Curve (AUC) of the ROC was .63 for predicting an ASD classification on the ADOS, .83 for the 3Di classification, and .82 for a classification on both the ADOS and the 3Di. For the teacher-report SRS the AUCs were .68 (ADOS), .63 (3Di), and .71 (ADOS and 3Di).

Conclusions: The parent-report and teacher-report SRS were only moderately related, suggesting that both informants provide some unique information. We found further support for the cross-cultural validation of the SRS. However, our preliminary results indicate that the parent-report SRS may correspond better to ASD classifications on standardised diagnostic instruments than the teacher-report SRS. We are currently investigating how the teacher-report SRS can contribute to the diagnostic assessment of ASD.

## 159 Medical and Psychiatric Co-Morbidity

**159.093 93** A Systematic Review of Interventions for Autistic Catatonia. D. Hare*, P. Bunton and H. DeJong, *University of Manchester*

Background: Around 8% of people with autistic spectrum disorders (ASD) present with catatonic symptoms, typically developing in mid-adolescence. Core features include being very still for long periods of time, getting 'stuck' when trying to do something, difficultly stopping actions once they have been started, difficulties in initiating actions, moving very slowly and taking a long time to finish actions and requiring physical and /or verbal prompts to finish actions. These symptoms have a significant impact on patients' quality of life and independence. Various treatments for autistic catatonia have been proposed, and treatment guidelines published. However, the existing literature is limited and has not been systematically reviewed

Objectives: The aim of the review was to systematically examine treatments that have been used to address catatonic symptoms in ASD, and to consider the evidence for the safety and efficacy of these interventions.

Methods: A systematic review of the existing literature was conducted, including search of three major online databases. Search terms included autism and catatonia, along with similar and related terms. Reference sections of included papers were hand searched for additional results. Any paper describing treatment of catatonic symptoms in at least one patient with an ASD was included in the review. So-called "grey literature" and non-English language papers were excluded. Study quality was also assessed and methodological limitations considered

Results: 22 papers describing a total of 28 cases were included in the final review, encompassing

both adult and paediatric cases. All papers described either single case reports or small case series. Treatments utilised included electroconvulsive therapy (ECT), various pharmacological interventions, behavioural and sensory interventions. Study quality was generally low, with particular limitations in outcome measurement, description of treatment and failure to control for confounding variables. There is some evidence for short term benefit of both electroconvulsive therapy and pharmacological interventions, particularly lorazepam. However, any benefit appears to be temporary and symptom remission is usually incomplete. Behavioural interventions also show some promise although evidence is currently limited to a very small number of cases. Side effects and adverse reactions were poorly addressed across the literature. Publication bias is also likely to be a significant issue.

Conclusions: Various treatments have been used to address catatonic symptoms in people with ASD, including ECT, pharmacological and behavioural interventions. However, the existing literature is limited to single case designs with serious methodological limitations. There is therefore little evidence to support any specific treatment. Behavioural interventions seem to show some promise, in that benefit may be better maintained than for other treatments and there is lower risk of serious side effects. Further research is needed to establish effective treatments for catatonic symptoms in ASD.

**159.094 94** Actigraphy in Children with Autism Spectrum Disorders: Strategies for Success. B. A. Malow*[1], D. B. Fawkes[1], S. Weiss[2], A. M. Reynolds[3], A. Loh[4], K. W. Adkins[1], D. Wofford[1], A. Wyatt[1] and S. E. Goldman[1], (1)*Vanderbilt Medical Center*, (2)*Hospital for Sick Children, University of Toronto*, (3)*University of Colorado Denver*, (4)*Surrey Place*

Background: The literature has been highly informative regarding actigraphy and its validity in pediatric research. However, minimal literature exists on how to perform actigraphy, especially in special populations including children with autism spectrum disorders.

Objectives: We determined whether providing comprehensive actigraphy training to parents increased the nights of actigraphy data that could be scored in a clinical trial. The training program covers the proper use of actigraphs in the home and recording on the sleep diary.

Methods: We compared two studies in children with autism spectrum disorders, both containing a behavioral sleep intervention in which actigraphy was the major outcome variable. The single site trial (Study 1) consisted of 20 children ages 4-10 years (80% male) whose parents received sleep education in a group setting at Vanderbilt University. The multisite trial (Study 2) consisted of 80 children ages 3-10 years (80% male) whose parents received either group or individual education at Vanderbilt University, University of Colorado Denver, or University of Toronto. Study 1 provided a basic level of actigraphy training while Study 2 provided more comprehensive actigraphy training using a variety of educational tools. Educational tools developed and implemented in Study 2 included presentation of actigraphy data to the parents, use of a quiz testing the parents' knowledge of actigraphy procedures, and a practice session in which the parents recorded data on sleep diaries and demonstrated proper use of an actigraphy watch, including the event marker. Feedback was given to the parents on their use of the watch.

One week of actigraphy was performed at baseline and post-intervention in both trials, and scored by a single analyst. The proportion of scorable nights of actigraphy was compared between Study 1 and Study 2 using Mann-Whitney U test.

Results: Scorable nights of actigraphy were higher in Study 2 than Study 1 at baseline ($P = 0.04$) and post-intervention ($p = 0.002$). The mean proportion of scorable nights (standard deviation) in the baseline and post-intervention phases was 0.91 (0.20) and 0.90 (0.17) for Study 2 compared to 0.73 (0.35) and 0.58 (0.39) for Study 1. One-way analysis of variance showed no difference in scorable nights between the three research sites in Study 2 [$F= 0.93$; $p = 0.4$].

Conclusions: Comprehensive training resulted in an increase in scorable nights of actigraphy. Our results support the use of educational tools to enhance actigraphy data collection in research studies involving children with autism spectrum disorders.

**159.095 95** Does Generalized Anxiety Predict Peer Relations in Youth with High Functioning Autism Spectrum Disorder?. K. Johnston* and G. Iarocci, *Simon Fraser University*

*Background:* A recent systematic literature review on anxiety in ASD revealed that prevalence rates

for anxiety range between 11% and 84%, with overall rates of anxiety disorder diagnosis at approximately 42% (White et al., 2009). Simonoff et al. (2008) found generalized anxiety to be one of the most commonly diagnosed comorbid disorders (13.4%) in ASD. Despite the high prevalence rate of generalized anxiety, there is a paucity of research examining the impact of these symptoms on social outcomes in high functioning (HF) youth with ASD. Furthermore, depression often co-occurs with anxiety, especially in HF youth with ASD, and may also have a negative impact on peer relations.

*Objectives*: The primary goal of this study was to examine the relations between parent ratings of generalized anxiety symptoms and peer relations in HF youth with ASD, including the degree to which generalized anxiety is predictive of peer relations. Because depression is often comorbid with anxiety and may also be associated with significant social difficulties, it was included in our analyses.

*Methods:* Fifty five youth with high functioning autism (i.e., IQ >85) between the ages of 7 and 18 were included. All relevant data were collected between 2007 and 2012 from youth and parents participating in research in the Autism and Developmental Disorders Lab at Simon Fraser University in British Columbia, Canada. Correlation analyses were used to test the relations between each of the predictor variables (generalized anxiety, depression, and social impairment) and covariates (age, IQ, and gender) with the outcome variable (peer relations). Multiple hierarchical regression analyses were conducted to examine whether a.) level of social impairment predicted peer relations after controlling for covariates, b.) generalized anxiety symptoms predicted peer relations after controlling for covariates and social impairment, c.) depression symptoms predicted peer relations after controlling for covariates and social impairment, d.) generalized anxiety symptoms predicted peer relations after controlling for covariates, social impairment, and depression. In this study social impairment was measured using the Social Responsiveness Scale (Constantino, 2005) and both generalized anxiety and depression symptoms were measured using the Behaviour Assessment System for Children, Second Edition (Reynolds & Kamphaus, 2004).

*Result*s: Although generalized anxiety was related to poorer peer relations, it was not predictive of peer relations over and above age, gender, IQ, autistic social impairment, or depression symptoms. However, IQ and depressive symptoms were strong predictors of peer relations in these youth. Overall, 38% of the sample scored in the clinically elevated range for generalized anxiety symptoms and many of these participants (42%) had a comorbid anxiety disorder diagnosis. In contrast, 55% of the sample fell in the clinically elevated range for depression, yet only two participants had a comorbid mood disorder diagnosis.

*Conclusions:* This finding highlights that depression symptoms, not generalized anxiety symptoms, are a predictor of poorer peer relations in youth with HFASD. This finding underscores the importance of screening for depression and other mental health issues in this population.

**159.096 96** Longitudinal Relations Among Anxiety, Sensory over-Responsivity and Abdominal Pain in Children with ASD. M. O. Mazurek*[1], A. Shui[2], R. A. Vasa[3] and A. Keefer[3], (1)*University of Missouri*, (2)*Massachusettes General Hospital for Children*, (3)*Kennedy Krieger Institute*

Background:

Children with autism spectrum disorder (ASD) often experience co-occurring medical and psychiatric symptoms. Among the most common are gastrointestinal (GI) problems, anxiety, and sensory over-responsivity (SOR). Although children with ASD are at greater risk for all three of these conditions, few studies have examined how these problems may inter-relate. Recent cross-sectional evidence indicates that SOR and anxiety are highly correlated among children with ASD, and that both of these problems are more common in those with ASD and chronic abdominal pain. There is also evidence that these problems may share similar underlying mechanisms, including HPA-axis involvement. These previous findings stress the importance of investigating these related problems jointly, and the need to examine the timing of symptom onset among children with ASD. Longitudinal associations among these variables in children with ASD have not been previously examined, however.

Objectives:

The purpose of this study was to examine the longitudinal relations among anxiety, SOR and chronic abdominal pain in a large, well-characterized sample of children and adolescents with ASD. Based on previous research among the general population, we hypothesized that anxiety and SOR would jointly predict the longitudinal occurrence of abdominal pain among children with ASD.

Methods:

Participants included 225 children and adolescents (ages 2-17) with ASD enrolled in the Autism Speaks Autism Treatment Network (AS-ATN) clinical registry database. Data were collected at baseline (T1) and at 1-year follow-up (T2). Measures included a demographic questionnaire, GI Symptom Inventory Questionnaire, Autism Diagnostic Observation Schedule (ADOS), Child Behavior Checklist (CBCL), Short Sensory Profile, and IQ testing.

Results:

Across the sample, 25.8% experienced chronic abdominal pain at T1 (defined as current abdominal pain, lasting 3 or more months), and of those 86.7% continued to experience abdominal pain at T2. An additional 23.8% of children without T1 abdominal pain went on to develop abdominal pain by T2. Baseline anxiety and SOR were significantly correlated ($p < .001$), and compared to children without abdominal pain, those with chronic abdominal pain had greater problems with anxiety ($p = .01$) and SOR ($p = .01$). Ordinal logistic regression models were used to examine longitudinal relations among variables. Among those without T1 abdominal pain, SOR was a significant predictor of developing chronic abdominal pain at T2 ($p = .002$). Among those with chronic abdominal pain at TI, neither anxiety nor SOR were significant predictors of abdominal pain at T2 (chronic vs. acute/no pain or chronic/acute vs. no pain).

Conclusions:

This was the first study to examine longitudinal associations among three common co-occurring problems in children with ASD. The results are consistent with emerging evidence that anxiety, SOR, and GI problems are inter-related for some children with ASD. In addition, SOR was a significant predictor of future development of abdominal pain, offering some preliminary information about the timing of these relationships and potential underlying mechanisms. Future work will continue to benefit from the use of longitudinal designs to examine these issues, as well as treatment studies to determine if targeted treatments can prevent or ameliorate all three conditions.

**159.097 97** Autistic Traits: A Highly Prevalent Risk Indicator for Childhood Abuse, Posttraumatic Stress, and Depression. A. L. Roberts*, *Harvard School of Public Health*

Background: Women with autistic traits (the "broad autism phenotype") may be at elevated risk for abuse in childhood. Children who noticeable differ from others are at increased risk of being targeted for abuse in childhood, as are children with communication impairments and children with disabilities. As depression and posttraumatic stress disorder (PTSD) are common sequelae of childhood abuse, women with autistic traits may be at elevated risk of these outcomes due to increased exposure to childhood abuse.

Objectives: To examine the association of autistic traits with childhood physical, emotional and sexual abuse, and depression and PTSD symptoms. To further examine the extent to which higher exposure to childhood abuse and lower social support explain possible associations between autistic traits and depression and PTSD.

Methods: We examined prevalence of childhood abuse, PTSD symptoms, and depression by autistic traits. We estimated odds ratios (OR) of childhood sexual abuse (Gallup Poll) and the highest quartile of childhood physical/emotional abuse (Conflict Tactics Scale) associated with quintiles of autistic traits in separate models. We modeled PTSD symptoms and lifetime depression as the dependent variables in separate models with autistic traits as the independent variable. To ascertain the extent to which childhood abuse and social support might account for possibly elevated risk of PTSD and depression in women with higher levels of autistic traits, we separately added childhood abuse and social support to models. In sensitivity analyses we restricted to women without a child with ASD (control mothers).

Results: Women in the highest versus lowest quintile of autistic traits were more likely to have been sexually abused (lowest quintile=26.7%;

highest quintile=40.1%) and to have experienced physical/emotional abuse (lowest quintile=14.3%, highest quintile=23.9%). PTSD symptoms and lifetime depression were also more prevalent in the highest versus lowest quintile of autistic traits (high PTSD symptoms, lowest quintile=4.5%, highest quintile=10.7%; depression, lowest quintile=7.9%, highest quintile=29.2%). Adjusted for covariates, women in the highest versus lowest quintile of autistic traits were at significantly elevated odds of sexual abuse (OR=1.7, 95% confidence interval (CI)=1.2, 2.6), and women in the top two quintiles of autistic traits were at elevated odds of physical/emotional abuse. Odds of PTSD were elevated in women in the top three quintiles of autistic traits compared with the reference group (OR range=1.4 to 2.0). Odds of depression were substantially higher in all women above the lowest quintile of autistic traits (OR range= 2.4 to 4.5). Adjustment for childhood abuse slightly to moderately attenuated associations with PTSD and depression. Social support did not further mediate these associations.

Conclusions: We identify for the first time autistic traits as a risk indictor for childhood abuse and PTSD. As we characterized autistic traits by quintiles among women without a child with ASD, our findings suggest that levels of autistic traits associated with elevated risk for depression and PTSD are highly prevalent in the general population. Risk of depression was approximately two to four and a half times greater in women above the lowest quintile of autistic traits and increased roughly monotonically with autistic traits.

**159.098 98** Anxiety, Distress, and Repetitive Behaviors in ASD, Anxiety Disorder, and Typical Development. K. Rump*[1], J. Worley[1], A. J. McVey[1], L. Guy[1], C. M. Kerns[2], H. Dingfelder[3], B. E. Yerys[1], M. Franklin[3], R. T. Schultz[4], J. Herrington[3] and J. Miller[1], (1)*Center for Autism Research, The Children's Hospital of Philadelphia*, (2)*Drexel University*, (3)*University of Pennsylvania*, (4)*The Children's Hospital of Philadelphia*

**Background:** Repetitive behaviors have been associated with DSM-defined anxiety in ASD using parent-report measures (Rodgers et al., 2012). However, this association has not yet been well studied using gold-standard, clinician directed measures of anxiety. It also has not been determined whether a similar association exists in individuals without ASD. Secondarily, some individuals with ASD experience high levels of anxiety-related distress and/or anticipatory worry around ASD-related challenges, such as difficulty with transitions, changes in routine, or exposure to social settings (Kerns et al., under review). This atypical distress may be a manifestation of anxiety in ASD that is not well represented in the DSM. We hypothesize that this atypical distress, like DSM-defined anxiety, may be associated with increased levels of impairing repetitive behaviors. In our studies of anxiety, we systematically differentiate DSM-anxiety from atypical distress often seen in ASD to provide a clearer discrimination of children with ASD and possible anxiety.

**Objectives:** To determine if repetitive behaviors are associated with anxiety in general, and if they are differentially associated with DSM-defined anxiety and the atypical distress often seen in ASD.

**Methods:** This ongoing study currently includes 67 children with or without ASD (ages 7-17). DSM-anxiety was assessed with the Anxiety Disorders Interview Schedule (ADIS); an addendum to the ADIS was designed to assess Atypical Distress. Caregivers also completed the Repetitive Behavior Scale - Revised (RBS-R). Participants fell into one of the following groups: Typically Developing Control (TDC); Anxiety Only (no ASD); ASD Only; and ASD+Anxiety (with specifiers DSM-Anxiety or Atypical Distress). Groups did not differ on age or IQ, as measured by the DAS-II. Separate DSM-anxiety and Atypical Distress severity scores were calculated for each participant using an algorithm to combine clinician severity ratings for DSM-IV anxiety and for atypical distress, respectively.

**Results:** One-way ANOVA analyses to date indicated a significant difference between groups on the RBS-R Overall Items Endorsed ($p<.001$). Post-hoc analyses showed that the TDC group was significantly lower than all other groups (M=1.4); while the Anxiety Only and ASD Only groups showed similar rates of repetitive behavior (M=9.6;M=9.9); and the ASD+Anxiety group had significantly higher levels of repetitive behaviors compared to all groups (M=15.6). To further explore the relationship between anxiety and repetitive behaviors in the ASD group, correlations between the RBS-R Overall Items Endorsed, DSM-anxiety severity score, and Atypical Distress severity score were computed. The RBS-R Overall

Items Endorsed was significantly correlated with Atypical Distress severity score ($r$=.50;p<.01).

**Conclusions:** Results suggest that individuals with clinical levels of anxiety demonstrate increased repetitive behaviors. This phenomenon was present among individuals with and without ASD. The higher rate of repetitive behaviors in the ASD+Anxiety group may reflect either the unusual manifestation of anxiety in some youth with ASD (e.g. atypical distress) or the potential overlap of atypical distress and repetitive behavior symptoms. It could also be that the RBS-R is capturing anxiety in addition to its intended purpose of capturing repetitive behaviors. Understanding the similarities and differences between atypical distress and DSM-defined anxiety is important for clinical care and research.

**159.099 99** Diurnal Cortisol and Daily Stress in Youth with Autism Spectrum Disorder. P. A. Renno*[1], L. J. Sterling[2] and J. J. Wood[3], (1)*University of California, Los Angeles*, (2)*UCLA Semel Institute for Neuroscience & Human Behavior*, (3)*University of California Los Angeles*

**Background:** While clinical experience suggests youth with autism spectrum disorder (ASD) experience increased levels of stress, few studies have investigated daily stressors and their potential relation to increased anxiety and ASD symptom severity in youth with ASD. Several daily stressors may be particularly relevant in ASD (e.g., the unpredictability of social interactions, sensory sensitivities to everyday environments). Further, there are few studies of HPA functioning in individuals with ASD and little research has examined the relation between cortisol levels and daily stress in individuals with ASD.

**Objectives:** To cross validate diurnal cortisol levels as a measure of stress in youth with ASD. A second objective is to examine the relation between daily stress, anxiety symptoms, and ASD symptom severity in youth with ASD.

**Methods:** Participants will include 40 high-functioning youth with ASD, aged 7-13 years. Thus far, cortisol levels have been collected for 26 youth, at four time points throughout the day for three days. Parent, child and diagnostician reports of daily stressors (e.g., Stress Schedule Survey), anxiety symptoms (e.g., Pediatric Anxiety Rating Scale), and ASD symptom severity (e.g., Social Responsiveness Scale) are collected.

**Results:** Preliminary findings suggest a relation between diurnal cortisol levels and parent report of daily stressors. A flattened diurnal cortisol slope was significantly related to increased parent reported stress related to sensory/personal contact ($r$ = -.44, $p$ < .05) and unpleasant events ($r$ = -.40, $p$ < .05). In contrast, the cortisol awakening response (CAR) was not significantly related to parent reports of stress. Daily stress and stressful life events were significantly correlated with increased anxiety, respectively ($r$ = .45, $p$ < .05; $r$ = .44, $p$ < .05). In particular, increased stress related to social and environmental interactions was significantly correlated with increased humiliation/rejection anxiety ($r$ =.47, $p$ < .05), social anxiety ($r$ =.46, $p$ < .05), separation anxiety ($r$ =.54, $p$ < .05) and total anxiety ($r$ =.58, $p$ < .01). The relation between stress, anxiety, and greater ASD symptom severity will be examined through mediational models.

**Conclusions:** Results thus far indicate that there is a relation between cortisol patterns and stress in youth with ASD, suggesting that cortisol may have the potential to serve as an objective marker of distress in a population marked by limitations in the ability to report emotional state. Further, greater daily stress was related to increased anxiety. Additional analyses will determine if greater daily stress and anxiety contributes to greater ASD symptom severity. Because ASD is a prevalent, disabling condition, it is of considerable importance to determine the factors that are associated with greater symptom severity and functional impairment. Stressors and anxiety ultimately could prove to be important targets of treatment for some youth with ASD as part of an overall intervention strategy for reducing core symptom severity and impairment.

**159.100 100** Exploratory Profile of High Functioning Adolescents and Adults with Autism Spectrum Disorders Experiencing Subthreshold Psychotic Symptoms. C. Wilson*[1], L. Kenworthy[1], L. G. Anthony[1], I. W. Eisenberg[2], B. Orionzi[2], A. Martin[2] and G. L. Wallace[2], (1)*Children's National Medical Center*, (2)*National Institute of Mental Health*

Background: In the general population, subthreshold psychotic symptoms are associated with impaired functioning, and increased rates of ADHD, depression, and anxiety. Less is known regarding these relationships within the context of autism spectrum disorders (ASD).

Objectives: The purpose of the current study is to assess the relative impact of caregiver-observed psychotic symptoms for adolescents and adults with ASD. We hypothesized that elevated subthreshold psychotic symptoms would be associated with greater difficulties in executive, adaptive, and social functioning. Subthreshold psychotic symptoms were also predicted to increase psychiatric complexity, as documented by elevated associations with other psychiatric diagnoses, such as ADHD, mood, and anxiety disorders.

Methods: Sixty-one adolescents and young adults (12-25 years) with high functioning ASD (Mean IQ=109.62; SD=15.35) participated in the study. Behavioral symptoms were assessed via caregiver report using the Adolescent Symptom Inventory-4 (ASI) or the Adult Inventory-4 (AI), which tap behavioral symptoms aligning with DSM-IV criteria for psychiatric disorders. The ASI/AI includes items assessing positive, negative, and disorganized schizophrenia symptoms. Pearson correlations were used to assess the strength of association between schizophrenia symptom severity and caregiver-reported executive function (BRIEF), adaptive functioning (ABAS-II), and social impairments (SRS). Linear regression was utilized to examine how schizophrenia symptom severity predicted severity of symptoms found in other DSM-IV disorders (i.e., ADHD combined, generalized anxiety disorder, major depressive disorder) based on the ASI/ASI severity scores.

Results: More than half of the sample (59.0%) endorsed at least one subthreshold psychotic symptom (Mean = 2.15; SD = 2.34). Schizophrenia severity scores were significantly correlated with age ($r$ = .40, $p$ = .001), overall executive function difficulties ($r$ = .33, $p$ = .01), greater social difficulties ($r$ = .38, $p$ = .002), and overall adaptive functioning ($r$ = -.39, $p$ = .003). IQ, race, and gender were not significantly associated with symptoms of psychosis. After adjusting for effects of age, schizophrenia symptom severity was associated with greater symptom severity associated with ADHD (Standardized Beta = 0.25; $t$ = 2.00, $p$ = .05) and generalized anxiety (Standardized Beta = 0.23; $t$ = 2.48, $p$ = .02), but not depression.

Conclusions: Adolescents/young adults with ASD experiencing subthreshold psychotic symptoms exhibit greater functional deficits including adaptive, executive, social, as well as more severe anxiety and attention problems than individuals with ASD alone. These behavioral difficulties indicate a potential point for early identification and possible intervention to ameliorate distress and dysfunction associated with subthreshold psychotic symptoms. Further research exploring the nature and validity of these subthreshold psychotic symptoms in the context of ASD is warranted.

**159.101 101** Attention Problems in ASD: Cognitive and Behavioral Correlates. C. J. Grantz*[1], A. P. Hill[2], E. Fombonne[2], D. A. Fair[2], J. Nigg[2] and J. van Santen[2], (1)*Oregon Health & Sciences University*, (2)*Oregon Health & Science University*

Background: Attention Problems are frequent in children with autism spectrum disorders (ASD; Gadow, DeVincent, and Pomeroy, 2006; Leyfer, Folstein, Bacalman, et al., 2006; Murray, 2010; Yerys, Wallace, Sokoloff, Shook, James, and Kenworthy, 2009). Some evidence has demonstrated a distinct phenotype of attention problems in conjunction with ASD, while some has instead found attentional difficulties to be a characteristic of the disorder.

Objectives: The current study examined whether the presence of attentional difficulties in a large sample of children with ASD represents a distinct phenotype of the disorder or is instead related to overall functioning.

Methods: Data were collected at the Oregon Health and Sciences University (OHSU; Portland, OR) site of the Autism Treatment Network (ATN). Data on 400 diagnosed subjects (83% male; mean age: 5.4 years; range: 2.0-16.9 years) were available. Attention problems were defined as clinical elevation ($T$>70) on the Attention Deficit/Hyperactivity Problems scale of the CBCL. This measure also provided scales related to symptoms of emotional and behavioral problems. Data on intellectual functioning, autism severity, verbal level, adaptive behavior, and socio-demographic variables were available via parent self-report and clinical interviews in the ATN database.

Results: Attention problems occurred in 26% of the children in this sample, consistent with previous findings of elevated prevalence of attentional difficulties in children with ASD. Clinically elevated attention problems were present significantly more frequently in children

with IQ less than 70 ($p$<.01). Attentional difficulties were associated with more impaired communication ($p$<.05) and daily living skills ($p$=.05) on the Vineland, but not with social abilities ($p$=.07). Severity of social and communication symptomatology ($p$=.09) and restricted and repetitive interests ($p$=.72) on the ADOS were not related to attention problems. Attention problems were significantly associated with other CBCL broadband and DSM scales, ranging from .27 (Anxiety Problems) to .59 (Oppositional Defiant Problems). Attention problems were not related to age ($p$=.91), gender ($p$=.35), parent education ($p$=.18), race ($p$=.84), language level ($p$=.14), or the use of complementary or psychotropic medication ($p$=.17).

Conclusions: In sum, attention problems, as measured by the parent-report CBCL, appear to be associated with greater cognitive and adaptive impairment, and were not related to ASD-specific symptomatology. A measure that differentiates ASD-specific attentional behaviors from behaviors indicative of ADHD should be considered to explore the etiology of attentional difficulties in children with ASD. Such a measure may better examine whether attentional difficulties in ASD represent a distinct phenotype of the disorder.

**159.102 102** Feeding Behavior & Comorbidity Differences for Children with and without ASD. D. L. Jaquess*[1], W. G. Sharp[2], R. Berry[2] and M. Cole-Clark[2], (1)*Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*Marcus Autism Center*

Background: Highly selective food preferences have been noted in individuals with an autism spectrum disorder (ASD), since such disorders were first described by Kanner (1943). In many if individuals, these restricted interests and related strong behavioral avoidance result in nutritional deficiencies and disrupted psychosocial development (Ledford & Gast, 2006). Although they may also suffer long-term health consequences, children without ASD's tend to present with difficulties related to inadequate oral intake, with less focus on selective food choices (Sharp, Jaquess, Morton & Herzinger, 2010). No researchers to date have compared initial clinical profiles that included direct behavioral observation of feeding disorder patients with and without comorbid ASD's.

Objectives: (a) Describe feeding patterns and medical conditions in children referred to a feeding clinic. (b) Compare and contrast profiles of children with and without ASD's.

Methods: Medical charts of 359 children (104 children with parent-reported diagnosis of ASD and 255 children without) who completed interdisciplinary evaluation (nutrition, speech/occupational therapy, behavioral psychology) of feeding difficulties were reviewed for medical history, oral-sensory and oral-motor functioning, and directly observed behavioral performance in mealtime. Measures were summarized and compared across diagnostic category.

Results: Significant differences observed for children with ASD included the following: reason for referral (more selectivity by type, and less food refusal), age (1.7 years older), fewer medical problems, fewer number of surgeries, elevated responding to sensory experiences, more problems with heightened sensitivity to sensory input, more sleep problems, less likely history of tube feedings (and related formula dependence), and fewer problems with overall caloric intake. No differences emerged in mean body mass index (BMI) z-scores, gestational age at birth, number of oral motor problems, reduced sensitivity to sensory experiences, or total number of prior therapy contacts for feeding. Both groups showed behavioral preferences for and against some foods, and the related behavioral topographies did not differ significantly under direct observation. With regard to total number of tolerated foods, however, children with ASD's did show greater restriction.

Conclusions: Children with ASD's share many similarities with other children who have feeding disorders related to divergent medical backgrounds, although the overall patterns of refusal differ. Therapists may be able to select intervention techniques primarily based on presenting complaint without regard to whether there is a comorbid ASD diagnoses. Nutritional impact of food selectivity among individuals with ASD's may require analysis of micronutrients to detect clinically significant deviations from recommended dietary intake.

**159.103 103** Genomic and Electrophysiologic Parameters Contribute to Clinical Endophenotypes in Autism and Epilepsy Populations. G. Barnes*, *Vanderbilt*

Background: Autism spectrum disorders (ASD) are known to have complex inheritance patterns such as copy number variants (CNVs), single gene disorders, and rare mutations of common synaptic genes. Alteration in interneuron enriched genes may explain why perturbations of GABAergic circuitry have been implicated in common neurodevelopmental disorders such as autism (ASD), intellectual disability, and epilepsy. Defects in GABAergic migration, cell numbers, and circuit formation are found in animal models of autism and epilepsy.

Objectives: Our central hypothesis is that temporal and spatial specific expression of GABAergic signaling pathways contributes to the influence of sleep disruption on epileptiform discharges and seizure expression in autism populations.

Methods: A unique database of autism epilepsy subjects (130), autism alone subjects (97), and epilepsy alone (150) was compiled by recording the genes in CNVs from clinical microarray data (CMA). These data from CNV genes were compared to all exon mutations from autism genetic studies published to date. The Gene ID numbers and UniProt IDs were recorded and then searched through the Gene Ontology (GO), KEGG, Pathways Commons, and WikiPathways databases to record interactions. Comparisons were made between ASD alone, ASD + partial epilepsy, and ASD + generalized epilepsy groups.

Results:

ASD + generalized epilepsy had a higher rate of detectable CNVs on clinical microarray testing (51%, p=0.05) than ASD alone (33%) or ASD + partial epilepsy (31%). The time at autism diagnosis was similar among the three groups. ASD + generalized epilepsy subjects had an older age of seizure onset (75 months, p=0.05) than ASD + partial epilepsy onset (52 months). ASD + generalized epilepsy subjects were significantly older when regression occurred (35 months, p=0.02) than ASD + partial epilepsy (25 months) or autism alone subjects (17 months). Individuals with epilepsy alone had an even younger age of seizure onset (39 months, p=0.007) and differed from autism populations in terms of polysomnogram parameters (total sleep time, waking after sleep onset, and sleep efficiency, p=0.04 to 0.007).

Meta-analyses of all four NGS papers yielded similar pathway results (including chromatin biology, cell to cell junction, cell adhesion categories, etc) to those already published [All adjusted p values were = or <0.009]. In contrast, only 6 genes among the 400+ genes from CNVs found in autism-epilepsy subject were found in common with all exon mutations published to date. Upon pathways analyses, some results were similar among all autism groups. However, pathways analyses suggest that there is a distinct set of enriched genes in CNVs from autism-epilepsy subjects including MAP kinase signaling, PAR1 mediated thrombin signaling, regulation of ARF GTPase signaling, diurnally regulated genes with circadian orthologs, prostaglandin synthesis and regulation, and transmission across chemical synapses. Notable genes deleted in CNVs from autism-epilepsy subjects including GABRB3, GABRG3, CHAT, and SLC18A3 (acetylcholine vesicle transporter) [all involved in interneuron function] were only found in subjects with ASD + generalized epilepsy.

Conclusions:

Taken together, these data suggest that distinct subgroups within the autism and epilepsy populations have associated genomic variants which may impinge strongly on function of unique neural circuits and expression of clinical endophenotypes.

**159.104 104** Good Night, Sleep Tight: The Impact of Early Bedtime Behaviors on Toddlerhood Sleep Problems in Infants at Heightened Risk for ASD. K. Spielman*[1], B. M. Winder-Patel[1], S. Thomas[1], J. Pandey[1], R. T. Schultz[1], S. Paterson[1] and .. The IBIS Network[2], (1)*The Children's Hospital of Philadelphia*, (2)*Autism Center of Excellence*

Background:

Previous work has demonstrated that children with Autism Spectrum Disorder (ASD) have difficulty falling asleep and staying asleep, which leads to decreased duration of sleep. These disturbances of sleep can impact daily learning and behavioral and emotional regulation (Souders 2009), which are marked deficits for those with ASD and the targets for early interventions. Sleep education and interventions have been documented to improve sleep and behavioral symptoms for those children with ASD (Malow 2013) yet little is known about the early sleep

characteristics that relate to later sleep problems in children with ASD.

Objectives:

To examine how early components of sleep and the methods used to put infants to sleep at 12 and 24 months impact sleep difficulties at 24 months.

Methods:

Data were collected from parent report measures of children at 12 and 24 months at one clinical site that were seen as part of a longitudinal study on the brain and cognitive development of infants at risk for ASD. Thus far, the data include 49 toddlers at high risk for ASD (HR) (mean age=24.54 months) and 21 typically developing low risk (LR) toddlers (mean age=24.34 months). We examined differences between groups on scores from the Sleep Problem subscale on the CBCL (*The Child Behavior Checklist for ages 1 ½ to 5 yrs*; Achenbach & Rescorla, 2000) and responses on the BISQ (*Brief Infant Sleep Questionnaire;* Sadeh 2004) including nighttime sleep duration, number of night wakings, duration of sleep onset, and the method and location of sleep onset and investigated how these variables correlated across development.

Results:

Our preliminary data reveal a significant increase in Sleep Problem scores for toddlers with ASD, a subset of 15 infants in the HR group, (M=59.33, SD= 10.728) as compared to LR toddlers (M=51.33, SD=3.168) at 24 months of age ($p<.05$). When we considered all high risk infants, this difference remained significant (HR mean score was 55.71, SD=8.631). In addition, correlations were examined for HR infants between BISQ data at 12 months and Sleep Problem scores at 24 months on the CBCL and indicated that duration of sleep onset (r= .566, $p<.05$) and number of night wakings (r= .695, $p<.01$) at 12 months correlate with CBCL Sleep Problem scores at 24 months. In addition, sleep problems at 24 months were significantly related to whether the child was put down for bed with support (i.e. rocking, feeding, and/or holding) or without support (r= .449, $p<.05$) and whether the child slept in their own bed or in their parent's or sibling's bed (r= .553, $p<.01$).

Conclusions:

These results indicate that there are characteristics of sleep as early as 12 months that relate to sleep problems a year later. Understanding these early characteristics may improve methods for sleep therapies and facilitate early intervention of sleep difficulties before reaching a level of clinical significance.

**159.105 105** Informant Agreement in ASD: Comparisons to Intellectual Disability. E. Stratis* and L. Lecavalier, *The Ohio State University*

Background: When assessing psychological and social functioning, the use of multiple informants is critical to obtain a comprehensive clinical picture. Differing environments, biases and expectations often influence reports from different informants. While agreement among informants has been widely studied in typically developing youth, research on this topic in youth with autism spectrum disorders (ASD) is limited.

Objectives: This study examined informant agreement in youth with ASD using a meta-analytic strategy while making comparisons to informant agreement in youth with intellectual disability (ID).

Methods: Following a comprehensive literature search, a meta-analysis was conducted to determine the average agreement among pairs of informants on rating scales that assess externalizing problems, internalizing problems and/or social skills.

Results: A total of 45 articles were located; 31 reported on informant agreement in youth with ASD and 14 reported on youth with ID. In youth with ASD, agreement on externalizing problems (weighted average $r$ = .41) was comparable to agreement on social skills (weighted average $r$ = .39), but significantly higher than agreement on internalizing problems (weighted average $r$ = .28). Similar results were found for youth with ID (externalizing weighted average $r$ = .44; internalizing weighted average $r$ = .36; social skills weighted average $r$ = .37). Within each behavior type and each informant pair, significant differences did not exist between youth with ASD and youth with ID. In youth with ASD, parents and teachers showed significantly lower agreement on internalizing problems (weighted average $r$ = .21) than did parents and self-report

(weighted average *r* = .48). Pairs of parents showed significantly higher agreement on social skills (weighted average *r* = .77) in ASD than did parents and teachers (weighted average *r* = .34), parents and self-report (weighted average *r* = .45) or teachers and self-report (weighted average *r* = .39). There were no differences among pairs of raters for externalizing problems in ASD.

Conclusions: Informant agreement in youth with ASD is consistent with that of youth with ID. Informants show higher agreement on externalizing problems and social skills than internalizing problems. Additionally, informant agreement on internalizing and externalizing problems as well as social skills in youth with ASD and ID is comparable to that reported in typically developing youth. Self-reports from youth with ASD or ID show agreement with parent and teacher reports similar to that found in typically developing youth, suggesting this is a potential source of clinical information. These results further highlight the importance of multiple informants in assessing behavior problems and social skills as each informant provides different but important information.

**159.106 106** Investigating Autonomic Nervous System Dysregulation in ASD. E. Anagnostou*[1] and A. Kushki[2], (1)*Holland Bloorview Kids Rehabilitation Hospital*, (2)*Bloorview Research Institute*

Background:

There is emerging literature to suggest that autism spectrum disorder (ASD) may be associated with dysfunction of the autonomic nervous system (ANS), although the nature of the dysfunction and its relation to ASD symptomatology are not well understood.

Objectives:

To investigate differences in ANS response to tasks eliciting core and co-morbid deficits of ASD between typically-developing children and those with ASD.

Methods:

A sample of typically-developing children (n=34, age: 12.5 +/-2.9 years, full-scale IQ: 112.6 +/- 14.2, 19 male), and those with a diagnosis of ASD (n=40, age: 12.0 +/- 2.9 years, full-scale IQ: 112.6 +/- 14.2, 33 male) completed five tasks to elicit behaviours associated with core deficits and co-morbidities of ASD: 1) Stroop test (performance anxiety), 2) public speaking task (social anxiety), 3) rapid visual information processing (RVP) test (attention), 4) stop-signal task (inhibition), and 5) the Reading the Mind in the Eyes test (theory of mind), as well as a physical activity task (treadmill walking). Each task was preceded by a baseline interval in which the participant watched a 5-minute animated movie clip. Throughout the experimental session, electrocardiogram (ECG) was measured and used to extract heart rate. Repeated measures multiple regression analysis was performed to examine the effect of group and group x task interaction on heart rate while controlling for age, gender, and full-scale IQ.

Results:

Multiple regression analysis showed a significant group x task interaction for heart rate (p=0.001). Posthoc analyses revealed that the heart rate increase in response to anxiety was significantly smaller in the ASD group compared to the typically-developing sample (Stroop task p=0.02, public speaking p=0.0004). No significant differences were found for other tasks. While heart rate was generally higher in the ASD group, these differences did not reach statistical significance.

Conclusions:

Our results suggest an atypical pattern of ANS function in ASD that is specific to the anxiety response. These results are consistent with ANS hyper-arousal in ASD.

**159.107 107** Longitudinal Course and Predictors of Aggression in Children with ASD. C. R. Engelhardt*[1], M. O. Mazurek[1], E. L. Wodka[2] and S. Kanne[1], (1)*University of Missouri*, (2)*Kennedy Krieger Institute*

Background: Although the nature, course, and predictors of aggression have been well researched in typically developing samples, there have been few large-scale studies of this topic in children with autism spectrum disorder (ASD). This is surprising given that aggression can have significant negative effects for individuals and families. Recent research on the prevalence and cross-sectional correlates of aggression in children with ASD suggests that several co-occurring problems are associated with aggression in this population, including sleep problems,

gastrointestinal problems, sensory problems, and self-injurious behavior. However, longitudinal studies examining the course of aggression and the variables that may predict change in aggression over time in children with ASD have not been conducted.

Objectives: 1) To examine changes in aggression over time among children with ASD, and 2) to investigate whether specific demographic, functional, or symptomatic factors predict changes in aggression over time among children with ASD.

Methods: Participants included children and adolescents (ages 2-18) with ASD enrolled in the Autism Speaks Autism Treatment Network (AS-ATN). The AS-ATN maintains a longitudinal clinical registry database, and data for the current study were collected at yearly intervals (enrollment, and first, second, and third annual follow-up visits). Data were available for 5,216 children at enrollment, with substantially fewer participants with complete data across all time points. Aggression was measured by the Aggressive Behavior Syndrome Scale from the Child Behavior Checklist (CBCL). Additional measures included demographic and parental concerns questionnaires, Autism Diagnostic Observation Schedule (ADOS), IQ, Children's Sleep Habits Questionnaire, Short Sensory Profile, and Vineland Adaptive Behavior Scales – Second Edition.

Results: Data were initially analyzed using an unconditional means model and unconditional growth model. These models suggested that: 1) children had different baseline aggression scores and rates of change, and 2) the average child in the sample had less aggression over time. Theoretically relevant predictor variables were then entered into hierarchical linear models (HLMs) in order to determine which variables accounted for variability in initial aggression scores and in changes in aggression over time. HLMs showed that higher initial aggression scores were associated with greater sleep problems, sensory problems, and self-injurious behavior, while GI problems were not associated with initial aggression scores. Results also indicated that specific sets of co-occurring symptoms predicted different rates of improvement in aggression over time.

Conclusions: Children with ASD show marked variability in initial levels of aggression and in how these behaviors change across time. Consistent with previous findings, the results indicate that co-occurring problems, including sleep problems, sensory problems and self-injury, are highly associated with aggression in children with ASD. Further, the current results indicate that these co-occurring problems may affect long-term improvement in aggression. This was the first large scale study to investigate longitudinal patterns of change in aggression in a large, well-characterized sample of children with ASD. The results provide important information about patterns of aggression and potential targets for intervention. Future longitudinal work should include more comprehensive measures of aggression, and should examine the extent to which treatment for aggression and co-occurring problems have reciprocal effects.

**159.108 108** Mental Health Disorders in High-Risk Younger Siblings of Children with Autism Spectrum Disorder. C. Roncadin*[1], J. A. Brian[2], S. E. Bryson[3], N. Garon[4], W. Roberts[5], I. M. Smith[6], P. Szatmari[5], T. Vaillancourt[7] and L. Zwaigenbaum[8], (1)*Peel Children's Centre*, (2)*Holland Bloorview Kids Rehab/ University of Toronto*, (3)*Dalhousie/IWK Health Centre*, (4)*Mount Allison University*, (5)*University of Toronto*, (6)*Dalhousie University / IWK Health Centre*, (7)*University of Ottawa*, (8)*University of Alberta*

Background: Mental health disorders are common in children with ASD, particularly anxiety and ADHD, but the prevalence and nature of mental health disorders among high-risk younger siblings of children with ASD is not yet known.

Objectives: The purpose of the current study was to describe mental health disorders in a sample of high-risk younger siblings of children with ASD.

Methods: Participants were 31 younger siblings of children with ASD from our Canadian multi-site prospective study who were followed from age 6 or 12 months to 8 years. Mental health diagnoses (other than ASD) were determined using the K-SADS-PL (2009 version), a semi-structured interview designed to assess current and past psychopathology in children age 6–18 years according to DSM-IV-TR criteria, administered to participants' parents. Chi-square tests were used to explore diagnostic rates between groups, and file review provided additional details about the cases with mental health diagnoses.

Results: Based on independent, best-estimate clinical diagnoses at age 8 made with the Autism Diagnostic Interview–Revised, Autism Diagnostic Observational Schedule, and expert clinical judgement using DSM-IV-TR, participants were classified as "non-ASD sibs" (n=17; 47% male) or "ASD sibs" (n=14; 79% male). The groups did not differ in language ability, as measured by the CELF-4 Core Language score ($t_{(26)}$=-1.36, p=.19). Overall, 29% (n=5) of non-ASD sibs and 64% (n=9) of ASD sibs met criteria for one or more lifetime diagnoses other than ASD, $Chi^2$=3.77, p=.05. Psychopathology primarily involved internalizing (mood and anxiety disorders), externalizing (attention-deficit and disruptive behavior disorders), and elimination disorders; no participant met criteria for schizophrenia/psychotic, eating, or tic disorders. The most common diagnosis among non-ASD sibs was Specific Phobia (n=3), whereas the most common among ASD sibs was ADHD (n=6). Anxiety disorders were evident in equivalent proportions in both groups (60% non-ASD sibs; 56% ASD sibs), $Chi^2$=1.31, p=.25.

Conclusions: This is the first known study of mental health disorders (other than ASD) in younger siblings of children with ASD. Consistent with previous studies of comorbidity in ASD, we found high rates of both internalizing and externalizing disorders among ASD sibs. Correspondingly, almost one-third of non-ASD sibs also had mental health disorders, and in both groups multiple disorders were common. These findings highlight the importance of monitoring mental health status in younger siblings of children with ASD throughout childhood, whether or not they have ASD themselves.

**159.109 109** Movement Abnormalities in Children with 16p11.2 Deletion or Duplication and Their Association with ASD and Other Neurodevelopmental Challenges.

K. Steinman*[1], R. Bernier[2], R. P. Goin-Kochel[3], L. N. Berry[3], K. Johnson[2], S. M. Kanne[4], A. Stevens[2], A. V. Snow[5], M. B. Ramocki[3], S. J. Spence[6], M. Proud[3], S. K. Kessler[7], E. Marco[8], L. Green-Snyder[6], W. Chung[9], E. H. Sherr[8] and E. Hanson[6], (1)*Seattle Children's Research Institute*, (2)*University of Washington*, (3)*Baylor College of Medicine*, (4)*University of Missouri Thompson Center for Autism & Neurodevelopmental Disorders*, (5)*Boston Children's Hospital, Harvard Medical School*, (6)*Boston Children's Hospital*, (7)*Children's Hospital of Philadelphia*, (8)*University of California, San Francisco*, (9)*Columbia University Medical Center*

Background: Motor abnormalities not identified by the traditional neurologic examination are seen with increased prevalence in autism spectrum disorders (ASD) and other neurodevelopmental disabilities (NDDs) not typically defined by their motor deficits, including speech and language disorders, attention-deficit hyperactivity disorder, and intellectual disability. Important insights into the neurobiological bases of NDDs can be obtained by examining the relationship between motor and cognitive function, but are complicated by the heterogeneity of NDD populations. The Simons Variations in Individuals Project is a research endeavor taking a "genetics-first" approach to studying a large cohort of individuals with 16p11.2 deletions (del) and duplications (dup) – recurrent copy-number variants (CNVs) that increase the risk of ASD and other NDDs – without regard to prior clinical behavioral/developmental diagnosis.

Objectives: To examine (1) if these genetically-identified populations have measureable motor problems not identified by traditional neurologic exam; (2) if such deficits are associated with ASD and ASD symptoms; intellectual disability; neurologic abnormalities; or other behavioral diagnoses seen in these populations; and (3) if the degree of motor deficit seen in these two populations differ independent of other identified neurodevelopmental factors.

Methods: The Movement Assessment Battery for Children – 2 was administered to 82 children with 16p11.2 del (n=49) or dup (n=33). One-sample t-tests were used to compare total standardized z-scores (MABC-T) in the del or dup groups to the general population and two-sample t-tests were used to compare MABC-T between del and dup patients. Two-sample t-tests and Pearson's correlation were used to assess for associations between MABC-T and various neurodevelopmental factors in del or dup groups. Multivariable linear regression models were used to examine the independent associations of MABC-T with neurodevelopmental factors while controlling for FSIQ, ASD, and the presence of dup vs del.

Results: Del and dup groups each exhibited low MABC-T compared to norm (-2.1 SD and -1.7 SD, each p<0.001; del versus dup: p<0.001). Higher Autism Diagnostic Observation Schedule-Calibrated Severity Score (ADOS-CSS) was associated with lower MABC-T in both groups (del:

r=-0.5, p=0.001; dup: r=-0.4, p=0.03), while diagnosis of ASD was only associated with worse MABC-T in del patients (p<0.005). In del, lower MABC-T was also associated with symptoms of appendicular weakness (p=0.04). In dup patients, lower MABC-T was also associated with lower FSIQ (r=0.6, p<0.001), articulation disorder (p=0.01), and hypotonia symptoms (p=0.03) and (truncal) signs (p<0.001). Neither language disorder nor ADHD were associated with MABC-T. FSIQ, ASD diagnosis, hypotonia (symptoms or signs), and the presence of dup (versus del) were all independently associated with lower MABC-T (all p≤0.04). ADOS-CSS was also an independent predictor of lower MABC-T when adjusting for FSIQ, ASD, and CNV, while diagnosis of articulation disorder did not survive adjustment for FSIQ and CNV.

Conclusions: Children with 16p11.2 del and dup have quantifiable movement deficits associated with multiple independent factors. There are differential associations of deficits with physical and cognitive abnormalities in del versus dup, as well as an independent association of motor deficits with presence of dup versus del.

**159.110 110** PGC Mega-Analysis of 5300 Individuals with ASD Yields a Genome-Wide Significant Association with the Astrotactin 2 (ASTN2) Gene. S. L. Santangelo*, *Maine Medical Center/Maine Med Ctr Research Institute*

Background: Presented on behalf of the Psychiatric Genomics Consortium: Autism Spectrum Disorder Working Group. Although copy number variants and rare mutations have been demonstrated to increase risk for ASD, empirical evidence supporting a large role for inherited common variants as risk factors for ASD risk is still lacking.

Objectives: In order to discover common variants that increase risk for ASD, the members of the Autism Spectrum Disorders Working Group of the Psychiatric Genomics Consortium conducted a large high-density genome-wide meta-analysis (mega-analysis) combining data from multiple genome-wide association studies on 6500 individuals with ASD.

Methods: The mega-analysis included data from six family-based studies across five different genotyping platforms. All raw genotype and phenotype data were uploaded to a central server and processed through the same quality control, imputation, and analysis procedures. Trios were converted to cases and matched pseudo-controls using PLINK_v1.07. Imputation was performed using SHAPE-IT/IMPUTE routines benchmarked against the 1000 genomes project (build v3.Aug2012). Individuals were excluded from analyses if they were assessed at less than 36 months old or if there was any evidence contradictory to an ASD diagnosis from the ADI-R and/or ADOS. The primary analyses were restricted to individuals of "European" ancestry, defined as having close similarity in genotype to the CEPH HapMap population (not simply geographic location). A total of 5305 individuals met diagnostic and ancestry criteria. Secondary analyses explored association with a strict autism diagnosis, cognitive ability, verbal status and gender. Association testing was carried out using logistic regression of imputed dosages. Analyses were performed using PLINK v1.07. Fixed effects meta-analysis was performed using METAL, weighted for the inverse standard error of the effect.

Results: We observed a genomewide significant association for the *ASTN2* SNP rs7026354 (OR=1.17; $p=6.7\times10^{-9}$). Each of the contributing studies reported an association in the same direction. In addition to the significant association with *ASTN2*, strong associations were observed with previously implicated ASD genes, including *EXT1* (rs7836146; OR=0.85; $p=9.16\times10^{-7}$) and *MACROD2* (rs6079556; OR=0.88; $p=2.18\times10^{-6}$). In a replication study using an independent set of 1500 cases and 51K controls, we observed effects in the same-direction for 19 of the 26 SNPs passing a threshold of p < 1x10-5, a statistically significant result (p=0.014). Exploratory analyses with alternate phenotypes yielded interesting, although not statistically significant, results.

Conclusions: In the largest genome-wide association study of ASD to date, we observed a single genome-wide significant association at the *ASTN2* locus on chromosome 9. *ASTN2*, a cell adhesion molecule expressed in the brain, is thought to have a role in neuronal migration. Rare copy number deletions in *ASTN2* have been observed previously in individuals with ASD. Results of this GWAS mega-analysis indicate that common variation is important and detectable in etiologic studies of ASD and contribute to genetic liability.

This work is presented on behalf of the Psychiatric Genomics Consortium: Autism Spectrum Disorder Working Group

**159.111 111** Parent and Teacher Perceptions of Emotional and Behavioral Problems in Children with ASD: Effects of Child Age and IQ. N. S. Raff*, S. S. Mire, A. N. Tagliarina, H. L. LeBlanc and H. Hyatt, *University of Houston*

Background: Youth with autism spectrum disorder (ASD) frequently experience comorbid emotional and behavioral problems, which may exacerbate ASD core symptoms. The Child Behavior Checklist (CBCL) often is used to capture parent-report of emotional and behavioral problems in youth with ASD. Yet such difficulties also manifest in school and impact programming/intervention decisions. Fewer studies focus on teacher-report of these symptoms, though the Teacher Report Form (TRF), a companion instrument to the CBCL, is available. Importantly, parent and teacher perceptions of problems may differ, including low (Internalizing scales) to moderate (Externalizing scales) CBCL-TRF agreement (Kanne et al., 2009). Effects of child age and IQ on parent-teacher reports of emotional and behavioral problems are equivocal. For example, prevalence of parent-reported anxiety and depression may increase with age and IQ (Mayes et al., 2011; van Steensel et al., 2011), while age and/or IQ may have little relationship with parent-reported externalizing behaviors (i.e., aggression) (Farmer & Aman, 2011; Kaat & Lecavalier, 2013). However, teacher-report of aggression may be higher for younger children with lower IQ (McTiernan et. al., 2011).

Objectives: To investigate a) cross-setting prevalence of clinically significant emotional and behavioral problems of youths with ASD (parent-, teacher-report); b) relationships between parent-teacher ratings; c) child age-related differences in ratings, while controlling for IQ.

Methods: Data from the Simons Simplex Collection (SSC) were analyzed ($N$=2760; age range 4.0-17.9 years [$M$=9.03, SD=3.57]). CBCL and TRF Composite scores (Internalizing; Externalizing) and syndrome scales were examined from preschool (ages 1.5-5; $N$=323) and school age forms (ages 6-18; $N$=903). Descriptive analyses characterized the type and prevalence of cross-setting emotional and behavioral problems; correlational analyses examined parent-teacher agreement. Dependent-samples $t$-tests examined differences between parent- and teacher-ratings. Forthcoming analysis includes one-way multivariate analysis of covariance (MANCOVA) to examine age-related CBCL-TRF differences while adjusting for IQ (covariate).

Results: Findings indicated more CBCL parent-ratings within the clinically-significant range ($t$≥64) for Internalizing (preschool: 36.0%, school-age: 38.4%) than Externalizing (preschool: 24.7%, school-age: 22.3%). Correlational analyses revealed low-to-moderate positive relationships between parent-teacher (e.g., CBCL-TRF) Internalizing and Externalizing scores, with higher correlations for Externalizing (preschool: $r$(321)=.27, $p$<.01; school age: $r$(900)=.36, $p$<.01) than for Internalizing (preschool: $r$(321)=.22, $p$<.01; school age: $r$(901)=.27, $p$<.01). Overall, CBCL-TRF syndrome scale correlations were higher for school-agers (range: $r$=.16 to $r$=.38) than for preschoolers(range: $r$=.07 to $r$=.33). Dependent samples $t$-tests indicated significant differences between parent- and teacher-ratings for Externalizing, but not Internalizing, in both preschoolers [$t$(322)=-2.22, $p$<.05, $r$=.27] and school-agers [$t$(901)=-4.82, $p$<.001, $r$=.36].

Conclusions: Preliminary analyses indicate differences in symptom manifestation across age-groups (preschoolers, school age) and between settings (home and school). We expect these findings to be further elucidated by exploring differences in CBCL-TRF scores by age-of-child (in years), adjusting for IQ scores (forthcoming MANCOVA). Parent-teacher agreement was higher for Externalizing than Internalizing symptoms for both age groups, with teacher-reported Externalizing behaviors significantly higher than parent-reported. These initial findings suggest differences in setting-specific demands or in peer-group comparisons. Both parent- and teacher-report of comorbid emotional and behavioral problems yield important information for supporting the cross-setting needs of youth with ASD.

**159.112 112** Parent-Reported Adjustment in Children and Adolescents with ASD: An Examination of Negative Cognitions, Executive Function, and General Cognitive Abilities. N. M. Reyes*, S. L. Hepburn, A. Blakeley-Smith, J.

Stern and J. Reaven, *JFK Partners/University of Colorado School of Medicine*

**Background**: Adjustment problems such as anxiety have been widely reported in individuals with Autism Spectrum Disorders (ASD; Leyfer et al., 2006). In non-ASD community and clinical samples, cognition has been found to play a role in the development and maintenance of internalizing and externalizing problems (Schniering & Rapee, 2002, 2004a, 2004b). Also, in one study with pre-schoolers, executive functions were found to predict with behavioral problems (Kim et al., 2013). However, only one study has reported an association between negative cognitions and anxiety and behavioral problems in adolescents with ASD (Farrugia et al., 2006). **Objectives:** The goal of this study was to examine the link between anxiety symptoms and behavioral problems and negative thoughts, executive function skills, and general cognitive abilities in youth with ASD. **Methods**: In this cross-sectional study, 59 school-aged boys (n=23), adolescent boys (n=27), and adolescent girls (n=9) participated in a comprehensive evaluation to assess anxiety and behavioral difficulties, cognitive abilities, and autism symptoms. Both parent and youth self-report measures were used to assess negative thoughts (i.e., Children Autonomic Thoughts; CATS), executive function (i.e., Behavior Rating Inventory of Executive Function; BRIEF), anxiety symptoms (Screen for Child Anxiety and Related Disorders; SCARED), and behavioral problems (Developmental Behaviour Checklist; DBC). Standardized cognitive testing was also completed using the Weschler Scales. **Results**: Correlations revealed three major findings. First, poor emotional control was associated with behavioral problems in young boys ($r$ = .39), as well as adolescent boys ($r$ = .52) and girls ($r$ = .94). Second, strong associations were found in girls, such that, negative thoughts were linked to panic ($r$ = .85), general anxiety ($r$ = .79), separation anxiety ($r$ = .87) symptoms, and school difficulties ($r$ = .84). Moreover, negative thoughts were linked to behavioral problems in young boys ($r$ = .54) and adolescent boys ($r$ = .37), but not in girls. Finally, general verbal ($r$ = -.51) and non-verbal ($r$ = -.74) cognitive abilities were associated with behavioral problems in adolescent girls only, such that lower general cognitive ability was a risk for more behavioral problems. **Conclusions**: The findings indicate that cognitions may play a differential role in internalizing and externalizing problems in boys and girls with ASD. Implications of the apparent links between negative cognitions, executive function, overall cognitive ability, and behavioral and emotional difficulties in youth with ASD will be discussed.

**159.113 113** Predictors of Adaptive Functioning and Internalizing and Externalizing Symptoms in Children with Autism Spectrum Disorder (ASD). D. Oosting*[1], K. A. Pelphrey[1], N. M. McDonald[2], H. Friedman[1], C. Keifer[1], C. Cordeaux[1], L. C. Anderson[3] and P. Ventola[1], (1)*Yale University*, (2)*Child Study Center, Yale University*, (3)*Yale Child Neuroscience Lab*

**Background**: Adaptive skills and maladaptive behaviors are important indices of a child's functioning. The existing literature has consistently demonstrated adaptive functioning deficits (Kanne et al., 2011) and a high prevalence of externalizing symptoms (e.g. aggression and hyperactivity) in children with ASD (Matson et al., 2009; Mayes et al., 2012). There is also evidence of elevated levels of internalizing symptoms (e.g., anxiety and depression) in this population (Mayes et al., 2011). Severity of autistic symptomatology and cognitive ability have been associated with adaptive skill delays (Klin et al., 2007; Lopata et al., 2012) and elevated levels of internalizing and externalizing symptoms (Jang et al., 2011; McTiernan et al., 2011), but these results have been inconsistently observed.

**Objectives**: We examined predictors of adaptive functioning, internalizing symptoms, and externalizing symptoms in a large sample of children with ASD. Our study is one of the first to include internalizing and externalizing symptoms as predictors of adaptive functioning. It is also one of the first to examine the predictors of maladaptive behavioral symptoms, particularly the less-studied internalizing symptomatology, in this population.

**Methods**: Participants included 200 children (6-17 years) with ASD. Cognitive abilities were assessed using the DAS-II ($n$ = 193), WISC-IV ($n$ = 5), or WASI ($n$= 2) (IQ = 91.9 ± 20.9, range = 50-146). Measures of autism symptom severity, internalizing and externalizing symptoms, and adaptive functioning were obtained from caregiver reports (Social Responsiveness Scale; SRS, Child Behavior Checklist; CBCL, and Vineland-II; VABS-II, respectively).

**Results**: Seventy-six participants (38%) exhibited marked elevations (T-score > 65) in internalizing symptoms, and 39 (19.5%) exhibited elevated externalizing symptoms, as measured by the CBCL Internalizing and Externalizing Problems domain scores. Adaptive functioning, measured by the VABS-II Adaptive Behavior Composite, was 75.9 ± 9.0 (range = 54-102), indicating that on average, our sample demonstrated significantly delayed adaptive skills. We conducted three structural equation analyses with adaptive functioning, internalizing symptoms, and externalizing symptoms as the dependent variables. More severe autistic symptomatology and lower IQ predicted more impaired adaptive functioning. Greater autism symptom severity and higher IQ predicted internalizing symptoms, while externalizing symptoms were predicted only by autism symptom severity. Though adaptive functioning was significantly correlated to both internalizing and externalizing symptoms, it was not predicted by, and did not predict, either symptomatology. Subsequent analyses will include an examination of the effects of child age on the generalizability of our findings.

**Conclusions**: Results suggest that autism symptom severity and cognitive ability are important factors in explaining individual differences in adaptive functioning, internalizing symptoms, and externalizing symptoms. Continued study is needed on the factors contributing to impairment in these domains, as they directly impact the daily lives of families and children with ASD. As we aim to improve long-term outcomes for these children, understanding the relationships between these areas of functioning may encourage and inform interventions that address both the factors that contribute to adaptive and behavioral functioning impairments and the deficits themselves.

**159.114 114** Prevalence of Obesity in Autism Spectrum Disorders and Associated Risk Factors. A. P. Hill*, K. E. Zuckerman, K. Asplund, Y. Yin and E. Fombonne, *Oregon Health & Science University*

**Background:** Obesity (OBY) is increasingly prevalent in childhood and adolescence, and is associated with medical problems, psychopathology, and impairments in functioning in typical populations. Children with autism spectrum disorders (ASD) may be at elevated risk for OBY for several reasons, including medication use and decreased physical social activities. However, few studies have examined behavioral and psychiatric risk factors associated with OBY in ASD.

**Objectives:** To examine predictors of OBY in a large clinical sample of children with ASD.

**Methods:** Participants included 5082 children with ASD ($M$= 6.1 years; range 1.6 – 17.4 years; 84.5% male) enrolled in the Autism Treatment Network (ATN). CDC and WHO gender-/age-specific cutoffs were used to classify children as OBY (BMI ≥ 95%) or not obese (NOB, BMI < 95%). Bivariate analyses were used to assess the association of OBY with socio-demographics, ASD severity, child functioning and behavior, medication use, and comorbidities.

**Results:** OBY prevalence was 17.9% overall, and ranged from 12.9% to 26.7% across ATN sites. In terms of socio-demographics, OBY prevalence was lower for children < 6 years than for those ≥ 6 years (16% vs 20.9%, $p$ < .001), and was unrelated to gender ($p$ = .9). OBY was positively associated with lower parental education ($p$ < .001), non-white race ($p$ = .01), and Hispanic/Latino ethnicity ($p$ < .001). There were no differences between OBY and NOB in terms of ASD symptom severity ($p$s > .4) as measured by ADOS Calibrated Severity Scores. In terms of cognitive levels, children with OBY were more likely to have IQ scores < 70 (34.9% vs 28%), and less likely to have scores ≥ 85 (45.9% vs 52%), compared to NOB children ($p$ = .01). OBY children also had significantly lower adaptive skills overall (Cohen's $d$ = .15) and in the communication ($d$ = .13), socialization ($d$ = .10), and daily living skills domains ($d$ = .08). In terms of medication use, OBY children were significantly more likely to take SSRIs (7.4% vs 4.8%, $p$ = .001) and atypical neuroleptics (8.0% vs 5.1%, $p$ < .001), but not amphetamines or melatonin ($p$s > .2). OBY children had significantly elevated sleep difficulties ($d$ = .14) and co-morbid emotional and behavioral problems as measured by the Child Behavior Checklist ($d$ = .13), including higher levels of affective ($d$ = .17), anxiety ($d$ = .09), and ADHD problems ($d$ = .07), but not oppositional defiant problems ($d$ = .02).

**Conclusions:** OBY was significantly associated with several socio-demographic variables and with increased use of certain classes of medication. OBY was also characterized by increased

difficulties in adaptive skills, communication, and sleep as well as elevations in depressive symptoms. However, ASD symptoms were not associated with OBY, suggesting that the some of the same risk factors apply for OBY occurring in ASD as in typical and other atypical populations. Interventions that take into account both general OBY risk factors as well as those that are ASD-specific, such as adaptive skills and comorbid depression, may hold promise for improved weight status in ASD.

**159.115 115** Retrospective Review of Dietary Intake in Children with an Autism Spectrum Disorder. M. Dole*[1], M. M. Cantor[2], M. Corkins[3] and K. A. McVicar[4], (1)*University of Tennessee Health Science Center*, (2)*Rhodes College*, (3)*University of Tennessee Health Science Center, Le Bonheur Children's Hospital*, (4)*University of Tennessee Health Sciences Center*

**Background:** Children meeting Autism Spectrum Disorder (ASD) DSM-IV criteria are characterized by impairments in socialization, language and communication, and restricted behavior repertoires. Many demonstrate restricted and repetitive diets. This may be compounded by specialty diets (i.e. gluten free casein free diet) known to increase risk of dietary deficiency. Dietary restriction has been noted, though the impact on overall nutrition has not been fully examined.

**Objectives:** To determine how many children known to have ASD report restricted dietary intake.

**Methods:** Retrospective chart review was performed on University Le Bonheur Pediatric Specialists, Inc., Pediatric Neurology medical records for children between the ages of 18 months and 18 years known to have an ASD listed as an ICD code in any of the first four diagnostic fields. Charts were identified and histories extracted for analysis using standardized questions prospectively applied to charts. Collection included demographic data and presence or absence of self or caretaker reported dietary restrictions, diagnosis of developmental delay, special education, speech, occupational or physical therapy and sleep difficulties. Data was analyzed for frequency, Wilcoxon rank sum comparisons, and associations, using Fisher's exact tests, to determine if identifiable characteristics of children were associated with a restricted diet or 'picky-eaters'.

**Results:** Two hundred-twenty-four charts were reviewed. Eighty-six (38%) contained information about diet. Mean age of children was 89.6 months (SD 46.8). Twenty-four (11%) reported having been on a special diet (6% on the GFCG diet). Fifty-three (24%) commented on eating habits and noted a limited diet or being a 'picky-eater'. Weak negative correlations were identified between age and self-restricted diet ($r=-0.14$; $p=0.21$), and between age and therapeutic dietary restriction ($r=-0.06$; $p=0.56$), though not statistically significant. No differences in presence or absence of developmental delay, use of speech, occupational or physical therapy, special education or sleep difficulties were noted. No difference in age between those with limited diets or picky eaters versus those not with limited diets or picky eaters were noted ($p=0.15$).

**Conclusions:** Thirty-eight percent of charts reviewed noted a dietary history. Though less than half of charts reviewed addressed diet, almost a quarter mentioned a limited diet or a 'picky-eater'. This suggests that diet and nutrition are a significant concern in these patients. The weak negative correlation noted between age and restricted diets or selective eaters and therapeutic dietary restriction suggests that these children are more likely to be younger in age, though this would need to be confirmed in a larger sample as the finding did not reach statistical significance. The impact of nutrition on early brain development has been well established. How ASD and restricted diets impact development in these children is unknown. Our pilot data suggests that many have restricted diets and that further studies of nutrition in these children may be warranted.

**159.116 116** Sleeping Disorders in Children with Autism Spectrum Disorders and Other Developmental Disabilities. M. D. Valicenti-McDermott*, K. Lawson, K. F. Hottinger, R. M. Seijo, M. Schechtman, L. H. Shulman and S. Shinnar, *Albert Einstein College of Medicine*

Background: Children with developmental disabilities(DD) experience sleep disorders at a higher rate than typically developing children. There has been a growing interest in characterizing sleep problems in children with special needs since interventions can improve sleep and may result in better daytime functioning and quality of life. Sleep problems are commonly reported by parents of children with Autism Spectrum Disorders (ASD) but information on

sleep disorders in ethnically diverse populations is sparse and there are few comparisons with children with other developmental disabilities.

Objectives: To compare reported sleeping difficulties in ethnically diverse children with ASD vs. those with other DDs and to assess the relationship of sleeping disorders with demographic factors.

Methods: Cross sectional study with structured interview for 50 children with ASD and 50 children with other DD, matched by age/gender. DDs included intellectual disability/global delay and cerebral palsy. Interview included the Child's Sleep Habits Questionnaire (Owens) and demographic factors. Sleeping disorder was defined as a score above 41 in the Total Sleep Disturbance Score. Statistical analysis included paired statistics, chi-square, t test, correlations and regression.

Results: Mean age 8 3 yr; 15% White, 44% Hispanic and 24% African/American. Sleeping disorder was reported in 78% of the ASD group and 34% of the DD group ($p<0.001$) and the Total Sleep Disturbance Score was significantly higher in the ASD group (49±7 vs. 44±9 p=0.01). Families of children with ASD reported higher scores in the areas of bedtime resistance(9.8±2 vs. 8±2 p=0.002), sleep anxiety(6.5±2vs.5.2±1.6p=0.001) and night wakings(3.9±1 vs. 3.3±0.9p=0.003) but there were no differences between the groups in the sleep duration, sleep onset delays, parasomnias, sleep disorder breathing or daytime sleepiness. Overall younger patients were more likely to present bedtime resistance (r-.26 p=0.008) and night waking (r-.22 p=0.027) but there was no other association between demographic characteristics and reported sleeping disorders within or across groups. The association between sleeping disorders and ASD persisted after adjusting for demographic characteristics, including maternal education, ethnic groups and time since diagnosis (OR 7.1 95%CI= 2.2-22.2).

Conclusions: In this ethnically diverse sample, parents of children with ASD reported more sleeping difficulties than children with other DDs, including bedtime resistance, sleep anxiety and night waking. There was no difference in sleep duration or parasomnias or daytime sleepiness between the groups. Therapy may be best targeted on these factors.

**159.117 117** Suicidal Ideation, Plans, and Attempts in Adults with Asperger Syndrome: A Clinic Referral Study. S. A. Cassidy*[1], P. Bradley[2], J. Robinson[3], C. Allison[1], M. McHugh[3] and S. Baron-Cohen[1], (1)*University of Cambridge*, (2)*Hertfordshire Partnership NHS Foundation Trust*, (3)*Cambridgeshire and Peterborough Foundation NHS Trust*

Background: Asperger Syndrome (AS) in adulthood is frequently associated with depression but there have been few studies exploring the lifetime prevalence of self-reported suicidal ideation (SI), plans and attempts (P/A) in this clinical group.

Objectives: 1) To quantify the life-time prevalence of SI in adults who were diagnosed at a clinic specializing in the late diagnosis of AS in comparison to other clinical groups; 2) To explore risk factors associated with life time prevalence of SI and P/A in this clinical group.

Methods: n = 374 adults diagnosed with AS at a specialist diagnostic clinic between 2004 and 2013 were screened for history of depression, SI and P/A prior to assessment using a self-report questionnaire, and completed self-report measures of autistic traits and empathizing. Rate of SI in the current sample was compared to published rates of SI in the general population and other clinical groups. Associations between depression, autistic traits, empathizing and likelihood of SI and P/A were also explored.

Results: Mean age at diagnosis was 31.5 years (range 17-67, SD=10.9). 66% of adults diagnosed with AS reported previous or current SI, 35% had planned or attempted suicide and 31.5% had depression. Adults with AS were 9.6 times more likely to report life time experience of SI than individuals from a general UK population sample ($\chi^2(1)=542.3$, $p<0.001$); 5.8 times more likely to report SI than a sample with one medical illness ($\chi^2(1)=238.5$, $p<0.001$); 3.6 times more likely to report SI than a sample with two or more medical illnesses ($\chi^2(1)=75.2$, $p<0.001$); 1.3 times more likely to report SI than a sample with psychotic illness ($\chi^2(1)=5.5$, $p<0.001$), but were not significantly more likely to report SI than a sample with drug dependency and ADHD ($\chi^2(1)=.001$, $p=.99$). Individuals with AS were 4.3 times more likely to report SI ($\chi^2(1)=27.8$, $p<0.001$) and 2.4 times more likely to report

planned or attempted suicide ($\chi^2(1)=14.3$, $p<0.001$) if they also had depression. Those who planned or attempted suicide also had a significantly higher level of self-reported autistic traits than those who did not ($t(366)=2.6$, $p<0.01$).

Conclusions: Individuals diagnosed with AS later in life are significantly more likely to report SI than other clinical groups. Depression and a high level of self-reported autistic traits are significant risk factors in life-time prevalence of SI and plans or attempts at suicide. This confirms anecdotal reports of increased rates of SI, and depression as a significant potential risk factor for suicidality in adults with AS. Individuals with AS often experience many risk factors (social isolation/exclusion, bullying in childhood and adolescence, academic underachievement, unemployment, employment difficulties, lack of a close confiding relationship, or no friends) that can cause low self-esteem and secondary depression. Given that many of these risk factors are avoidable, the secondary depression may be preventable. This highlights the need for further research exploring the effect of appropriate service planning and support for adults with AS on the prevalence of secondary depression and suicidality.

**159.118 118** Symptoms of Autism in Children with ADHD with and without Concerns for ASD. R. L. Grzadzinski*[1], C. Lord[2] and S. L. Bishop[3], (1)*Weill Cornell Medical College & NY Presbyterian Hospital/Westchester Division*, (2)*Weill Cornell Medical College*, (3)*Center for Autism and the Developing Brain, Weill Cornell Medical College*

Background: Research has indicated that some individuals may present with both Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD), though the overlap of the two disorders varies across studies. Changes from DSM-IV to DSM-5 allows for an individual to receive co-occurring diagnoses of ASD and ADHD. Nevertheless, clinicians often struggle to distinguish social difficulties associated with ADHD from social difficulties associated with ASD. Thus, further research into the differential diagnostic presentations of these two disorders is warranted.

Objectives: To compare ASD symptoms, measured by the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview (ADI-R), in two groups of children who ultimately received diagnoses of ADHD: 1. Children with ADHD who received an evaluation for ASD due to parental concerns about ASD (ADHD+concerns) and 2. Children with ADHD who received an evaluation for ASD as part of a research study although the parents had no concerns about ASD (ADHD-concerns).

Methods: The overall sample consisted of 106 children (78 males) diagnosed with ADHD (based on standard measures and clinician formulation) with a mean age of 8.4 years (+ 3.4). Of the overall sample, 49 children (40 males) were in the ADHD+concerns group and 57 children (38 males), recruited from an ADHD clinic, were in the ADHD-concerns. Chi-square and ANOVAs compared the groups; to correct for multiple comparisons, a significance threshold was set at a=0.01.

Results: The ADHD+concerns group scored significantly higher on total scores across social [$F(1, 99)=17.63$, $p<0.001$], communication [$F(1, 99)=27.60$, $p<0.001$], and restricted/repetitive behaviors/interests [$F(1, 99)=23.73$, $p<0.001$] domains of the ADI-R. In the social domain, 12 (21%) of the ADHD-concerns and 24 (55%) of the ADHD+concerns met cut-offs for ASD [significant difference between groups, $X^2(1)=12.14$, N=101, $p<0.001$]. In the communication domain, 16 (28%) of the ADHD-concerns and 28 (64%) of the ADHD+concerns met cut-offs for ASD [significant difference between groups, $X^2(1)=12.78$, N=101, $p<0.001$]. In the restricted/repetitive behaviors/interests domain, 19 (33%) of the ADHD-concerns and 32 (72%) of the ADHD+concerns met cut-offs for ASD [significant difference between groups, $X^2(1)=15.42$, N=101, $p<0.001$]. Eighteen (32%) children in the ADHD-concerns and 12 (24%) in the ADHD+concerns met cut-offs for ASD on the ADOS [no difference between groups, $X^2(1)=0.65$, N=106, $p=.42$]. Two (4%) children in the ADHD-concerns and 3 (7%) in the ADHD+concerns met cut-offs for ASD on the ADOS *and* the ADI-R [no difference between groups, Fisher's exact test, $p=.38$]. No significant differences in gender, age, verbal/nonverbal IQ, ADOS scores, and symptoms of hyperactivity (on the CBCL) were found between the two groups. Analyses will be presented to elucidate specific differences between groups.

Conclusions: These results indicate that, based on standardized diagnostic measures, some children with ADHD present with symptoms of ASD. Not surprisingly, parental reports of ASD symptoms (ADI-R) in children with ADHD may be especially elevated in children whose parents have specific ASD concerns. This highlights the importance of gathering information from multiple sources, especially a trained clinician, when assessing ASD in ADHD children.

**159.119 119** The Impact of Demographics and Sleep Hygiene on Sleep in Children Aged 2-5 Years with and without Autism Spectrum Disorder (ASD). A. L. Richdale*, *La Trobe University*

Background: Poor sleep in children is often related to bedtime associations and routines, behavioural issues surrounding sleep, or night time fears. Socio-cultural factors including culture, education and family income, and sleep hygiene factors, including the sleep environment, bedding and night wear, screen time, and meals can also affect children's sleep, but their impact is less commonly explored, particularly in young children.

Objectives: To investigate relationships between family demographics, environmental factors and caregiver-reported sleep difficulties in children aged 2- to 5-years with and without ASD.

Methods: Participants were the primary caregivers ($N$ = 96) of 101 children (63 boys, 34 girls), mean age 47.5 months ($SD$= 12.9 months), including 28 children with ASD and 2 children with developmental delay. Caregivers completed a survey including a demographic questionnaire, an environment and sleep questionnaire, and the Children's Sleep Habits Questionnaire (CSHQ). Group comparisons (children with a sleep problem, children with no sleep problem; typically developing (TD) children, children with ASD), chi-square, and correlations were conducted as appropriate. Regression models were also conducted to examine predictors of CSHQ total score and daily total sleep.

Results: 55.4% of the children had a sleep problem (79% of the children with ASD; 46.5% of TD children), and the average CSHQ total score was higher in these children than in children without a reported sleep problem ($p$ < .001). CSHQ scores did not differ with age or diagnosis. Younger children slept more than older children ($p$ < .001), and children with ASD and a sleep problem slept less than other children ($p$ < .05). Total CSHQ score was related to family income, and primary caregiver employment and education. CSHQ score and total sleep were each related to a range of sleep hygiene variables including temperature, screen time, bed covers and night wear. Hierarchical multiple regressions with CSHQ total score and total daily sleep as dependent variables were conducted. The final models were significant; screen time, temperature and bedcovers together significantly accounted for 28% of the variance in CSHQ total score, while age, ASD diagnosis, screen time and sleep environment significantly accounted for 44% of the variance in hours slept.

Conclusions: These results indicate the importance of demographic and sleep hygiene factors on sleep problems in toddlers and pre-school children, regardless of whether the child has an ASD. While ASD impacted negatively on total sleep in this age range, children with and without ASD had similar sleep problem scores. The results support that attention to screen time (television and computers/tablets), the bedroom environment and bedding are important for good sleep. It was surprising that even at this young age screen time impacted on children's sleep. In particular, tablet (e.g., ipads) use by children with ASD is popular, with an increasing number of apps available for young children. Tablet use may be a new factor contributing to poor sleep in young children with ASD especially as the children with ASD in this study spent twice as much time as the TD children on computers/tablets.

**159.120 120** The Prevalence of Neurofibromatosis Type 1 Among Children Identified with Autism Spectrum Disorders By the Autism and Developmental Disabilities Monitoring (ADDM) Network. D. Bilder*[1], A. V. Bakian[1], D. Stevenson[1], P. Carbone[1], C. M. Cunniff[2], A. B. Goodman[3], W. M. McMahon[1] and D. Viskochil[1], (1)*University of Utah*, (2)*University of Arizona*, (3)*Centers for Disease Control and Prevention*

Background: Neurofibromatosis Type 1 (NF1) is a neurocutaneous disorder characterized by café-au-lait spots, neurofibromas, and optic gliomas. Neurodevelopmental disorders associated with NF1 include Autism Spectrum Disorders (ASD), learning disabilities, attention deficit hyperactivity disorder (ADHD), and intellectual disability (ID). Recent studies have identified ASD symptoms in up to 27% of patients with NF1. The frequency and pattern of DSM-IV criteria and associated ASD

characteristics in children with co-occurring ASD and NF1 (ASD/NF1) have not previously been examined in a population-based sample.

Objectives: (1) to determine the prevalence of NF1 in a population-based sample of 8 year-old children with ASD, and (2) to identify and compare patterns of ASD criteria and related characteristics between children with ASD/NF1 and ASD only.

Methods: The Autism and Developmental Disabilities Monitoring (ADDM) Network identified 8-year-old children with ASD using validated population-based, multi-source records review methods during surveillance years 2000, 2002, 2004, 2006, and 2008. The ASD/NF1 group included ASD cases for which a NF1 diagnosis and/or ICD9 code (237.71) were indicated in their records. Differences in characteristics between ASD cases with and without NF1 were tested using $\chi 2$ and t-tests. Characteristics that were compared included sex, race/ethnicity, ID, ADHD, epilepsy, developmental regression, age of regression onset, ASD classification, ASD community diagnosis, and DSM-IV diagnostic criteria patterns. For DSM-IV criteria and pre-existing ASD community diagnosis comparisons, samples were restricted to surveillance years 2000, 2006, 2008 for which complete data were available.

Results: Among 12,271 children who met DSM-IV ASD diagnostic criteria, 22 (0.17%; 95% CI: 0.12%-0.27%) had NF1 /ASD. There was no difference in the distribution of sex or race/ethnicity between children with ASD/NF1 and ASD only. There was no difference in the frequency of history of regression or the co-occurrence of ID, ADHD, or epilepsy with ASD, although a lower frequency of co-occurring ID in children with ASD/NF1 than with ASD only was nearly statistically significant (p=0.06). Significantly fewer (p=0.04) children with ASD/NF1 had a previous ASD community diagnosis (53%), compared to children with ASD only (76%). Children with ASD/NF1 (58%) were significantly less likely (p=0.001) than those with ASD only (84%) to meet diagnostic criterion 1a (difficulty using or understanding non-verbal communication). A small difference was observed between ASD/NF and ASD groups in mean number of DSM-IV criteria met (8.4 and 8.9 respectively, p=0.44); no difference between groups was found in the median number of criteria (9).

Conclusions: The estimated NF1 prevalence among 8-year-old children with ASD was approximately 5 to 7 times higher than published general population prevalence estimates (1-in-3000 to 1-in-4000). The actual prevalence may exceed this because the presence of a co-morbid NF1 diagnosis is not consistently collected across ADDM sites. Among children with ASD/NF1, the lower prevalence of co-occurring ID and likelihood of a previously established community ASD diagnosis suggest that those with ASD/NF1 may have milder ASD manifestations than children with ASD only. These findings underscore the importance of regularly evaluating children with NF1 for ASD.

**159.121 121** The Relationship Between the Core Features of ASD and Maladaptive Behaviours Measured Using the Diagnostic Interview for Social and Communication Disorders. R. G. Kent*[1], A. S. Le-Couteur[2], J. Gould[3], L. Wing[3] and S. R. Leekam[1], (1)*Cardiff University*, (2)*Newcastle University*, (3)*National Autistic Society*

Background: One in four children with ASD are reported to meet diagnostic criteria for Oppositional Defiance Disorder or Conduct Disorder and aggression affects 53% of individuals with ASD. The Diagnostic Interview for Social & Communication Disorders (DISCO) is a semi-structured diagnostic interview, that focuses on symptoms relevant for an ASD diagnosis (social communication and repetitive, restricted behaviours) and items measuring other behaviours necessary for a broader range of co-morbid conditions such as attention deficit hyperactivity disorder (ADHD), pathological demand avoidance (PDA), Catatonia, Tic disorders, developmental coordination disorder (DCD) and a range of maladaptive behaviours.

Objectives: The aims of the current study were to: establish the reliability and factor structure of the maladaptive scale of the DISCO; compare the rates of challenging behaviours in individuals with ASD in comparison to clinical and typically developing controls; and determine the relationship between maladaptive behaviours and core features of ASD. Additional analyses assessed the correlations between maladaptive behaviours and DISCO defined co-morbid conditions.

Methods: Two UK datasets were used. Sample 1 - 36 individuals with ASD, 31 clinical comparison controls (18 individuals with an intellectual disability 17 with a language impairment) and 15 typically developing controls. Sample 2 -200 DISCO interviews of individuals referred to a UK national ASD assessment centre.

Results: The 16 maladaptive behaviour items in the DISCO created a reliable scale (Cronbachs α = .92,), the maladaptive total score was significantly higher in the ASD group than the clinical or typical control groups. Maladaptive behaviours were significantly predicted by core ASD domain scores as measured using the DISCO. Principal Components Analysis resulted in a two factors solution: *behaviours affecting other people* (ten items; e.g. behaviour in public places, wanders, lack of co-operation) and *communicative disruptive behaviours* (six items; e.g. interrupts conversations, talks to strangers). Scores for both factors significantly differed between the diagnostic groups. Regression analyses revealed the first factor was significantly predicted by social interaction score; the second by both communication and repetitive behaviour scores as well as age.Maladaptive behaviour score was positively associated with the number of co-morbid conditions as identified using the DISCO. Both maladaptive factors were positively related to PDA, catatonia and ADHD scores, whereas TIC disorder scores were related to "behaviours affecting other people" only and scores for DCD were related with the "communicative disruptive" factor only.

Conclusions: This data support the prevalence of maladaptive behaviours in ASD and identifies sub-groups of these behaviours that have different associations with the core features of ASD. Individuals with high rates of maladaptive behaviours also appear to have more behaviours associated with co-morbid clinical conditions. The DISCO is a semi-structured interview that provides a framework for collecting parent/carer information on behaviours relevant for a diagnosis of ASD and a much broader range of behaviours required when considering possible co-occurring conditions. This diagnostic tool has potential benefits for clinical and research practice.

**159.122 122** The Role of Hypersensitivity in Anxiety and Specific Phobia in ASD. C. M. Kerns*[1], T. Rosen[1], J. Herrington[2], J. Miller[3], R. T. Schultz[4] and J. E. Connell[1], (1)*Drexel University*, (2)*University of Pennsylvania*, (3)*Center for Autism Research, The Children's Hospital of Philadelphia*, (4)*Children's Hospital of Philadelphia*

Background:

Research indicates that anxiety disorders occur in 40% of youth with an ASD (van Steensel et al., 2011), and sensory abnormalities inherent to ASD may predispose youth to various manifestations of anxiety (Green & Ben-Sasson, 2010). Hypersensitivity to sensory stimuli has been associated with anxiety in youth with and without ASD (Pfieffer et al., 2005; Reynolds et al., 2005) and may be related to the development of traditional and unusual specific phobias in ASD (Koegel et al., 2004). Hypersensitivity may increase the likelihood that individuals become overwhelmed by and avoidant of specific stimuli – a trajectory that can lead to the development of specific fears and other anxiety concerns (Bellini, 2006). Whether sensory abnormalities are differentially related to the presentation of specific phobias versus other anxiety disorders in ASD is unknown, though testing this hypothesis will have important implications for anxiety prevention and treatment.

Objectives:

To assess the relationship of hypersensitivity to anxiety in ASD, and specifically to phobia, this study will examine parent reports of hypersensitivity in individuals with ASD alone (ASD group), ASD and specific phobia (ASD+Phobia group), and ASD and other anxiety disorders (e.g., social phobia, separation anxiety and generalized anxiety disorder; ASD+ANX group).

Methods:

Participants were 53 youth (ages 7 – 17 years, *M*=10.59, *SD*= 2.81) diagnosed with ASD (79% male) as determined by the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & LeCouteur, 1994), Autism Diagnostic Observation Scale (ADOS; Lord et al., 2000) and clinical judgment. All participants had a verbal IQ of 60 or greater on the Differential Ability Scales (DAS-II; Elliot, 2007). Forty-nine percent were taking medication. Hypersensitivity was measured via Likert ratings from the sensory sensitivity subscale of the parent-report Sensory Profile (Dunn, 1999). The Anxiety Disorders Interview

Schedule- Child and Parent Versions (ADIS-C/P; Silverman & Albano, 1996) assessed anxiety disorders and specific phobias. Analysis of covariance assessed differences in parent-reported sensory sensitivity by group (ASD alone, ASD + ANX, ASD + Phobia), controlling for medication status.

Results:

Results indicated significant differences in sensory sensitivity between groups $F\ (1, 49) = 6.38$, $p = .003$, controlling for medication status, $F\ (1, 49) = 3.65$, $p = .06$. Post hoc contrasts indicated significantly increased sensory sensitivity in ASD+Phobia group (M = 4.35) versus the ASD group (M = 3.5; $p = .003$). By comparison, there were no significant differences between the ASD+ANX (M = 3.72) compared to ASD+Phobia or ASD groups. Additional item-level analyses are planned to detect symptoms underlying these associations and potential diagnostic overlap.

Conclusions:

These preliminary findings indicate that specific phobia in ASD is associated with hypersensitivity to sensory stimuli. Hypersensitivity ratings were lowest for the ASD group and highest for the ASD plus phobia group, with ratings for youth with ASD and other anxiety disorders falling in the middle. Whether associations between anxiety and hypersensitivity in ASD reflect a true, theoretically informative relationship or a function of symptom overlap will be explored.

## 160 Social Cognition and Social Behavior

**160.123 123** A Longitudinal Investigation of Parent Reported Social Functioning in Autism Spectrum Disorders: Still Lots of Room for Improvement. K. M. Dudley*[1], G. L. Wallace[2], L. G. Anthony[3], C. E. Pugliese[3], Y. Granader[3], A. C. Armour[3], B. Orionzi[2] and L. Kenworthy[3], (1)*Children's National Medical Center,*, (2)*National Institute of Mental Health*, (3)*Children's National Medical Center*

Background: The current diagnostic framework for autism spectrum disorders (ASDs) emphasizes social impairments, but also notes impaired executive function (EF). There is some evidence for the interdependence of EF and social cognition in the development of early social skills, but little is known about how social functioning (SF) and EF contribute to social outcomes in ASD without intellectual disability.

Objectives: This longitudinal study investigates the trajectory of parent-reported SF in ASD and explores the impact of baseline SF and EF on that trajectory. Specifically, this study investigates whether parent-reported EF and SF at baseline predicts changes in SF over time. We predicted that SF would improve over time in this group of high functioning children with access to clinical services; and that EF at Time-1 would correlate positively with improvement in SF over time.

Methods: Participants were 38 children, adolescents, and young adults diagnosed with ASD (*M* FSIQ=107.25) who had two or more clinical or research evaluations (*M* age Time-1=13.80 ±3.70; *M* age Time-2=16.96 ±4.23) occurring at least six months apart (*M*=3.21 years). SF and EF were assessed through parent report on the Behavior Rating Inventory of Executive Function (BRIEF, Global Executive Composite (GEC) T-score) and the Social Responsiveness Scale (SRS, Total T-score). Reliable change indexes (RCIs) were calculated for each participant to determine whether change in SF from Time-1 to Time-2 was clinically significant at the 95$^{th}$ confidence interval. Lastly, correlation coefficients controlling for age were conducted to assess the relationship between total SF and EF at Time-1 and the change in SF between Time-1 and Time-2.

Results: RCI calculations indicated that 28 participants did not improve in SF (no change *N*=24; deteriorated *N*=4) and 10 participants significantly improved between Time-1 and Time-2. There was a significant negative relationship between SF change scores and SF scores at Time-1 ($r(33)=-.646$, $p<001$). Analyses also revealed a significant positive correlation between BRIEF GEC scores and total SF scores at Time-1 ($r(33)=.395$, $p=.019$), but not between GEC scores at Time-1 and SF change scores.

Conclusions: These data indicate that only 26% of children with ASD improved in parent-reported SF over time, and that those who improved began with significantly more impaired SF than those who did not improve. Perhaps those most impaired individuals at Time-1 received more intensive interventions, a question to be addressed in future research. Alternatively these data may represent the effect of statistical regression to the mean, in that only those who began with especially elevated social impairment

improved over time. This overall lack of improvement in social abilities may have ultimately affected the study's power to view the true relationship between EF and SF, as EF did not impact the SF trajectory as expected. EF did, however, relate to SF at Time-1, suggesting the need for further exploration of the relationship between these key developmental domains. Overall, this study illustrates a lack of improvement in SF, even in those with access to good clinical care, underscoring the need for the continued development of evidence-based interventions.

**160.124 124** Pupillary Responses to Emotional Faces in Individuals with Autism Spectrum Disorder and Their Unaffected Siblings. A. L. Hogan-Brown*, J. Barstein, S. J. Shah, C. Stiehl and M. C. Losh, *Northwestern University*

Background: From a young age, individuals with ASD look less at faces than their typically developing peers. However, little is understood about the underlying cognitive and neurobiological mechanisms that contribute to this decreased attention. The pupillary response (i.e., change in pupil dilation) is regulated by the autonomic nervous system and is directly associated with amygdala activity. In a recent study, individuals with ASD demonstrated attenuated pupillary responses as they viewed happy faces, providing preliminary evidence of reduced autonomic arousal in response to social-emotional information. However, it is unclear whether this response is present when viewing neutral or fearful faces. Furthermore, no studies have investigated pupillary responses in first-degree relatives of individuals with ASD (e.g., unaffected siblings). Understanding the relationship between visual attention and pupillary responses to faces in individuals with ASD and their first-degree relatives is an important step toward elucidating the role of autonomic arousal during social-emotional information processing.

Objectives: To investigate looking patterns and pupillary responses in individuals with ASD and their siblings as they view emotional faces.

Methods: Eleven individuals with ASD (mean age = 15.48), eight siblings of individuals with ASD (mean age = 13.01), and 10 typically-developing controls (mean age = 15.62), have participated in this study to date (with additional participant testing underway). Participants passively viewed 18 trials each of happy, calm, and fearful faces, taken from the NimStim Stimulus Set (Tottenham et al, 2009). A Tobii X60 eye tracker recorded eye movements and pupil dilation. Each trial lasted 3 seconds and was preceded by a scrambled, luminance-matched version of that trial. Looking time on the eyes, nose, mouth, and entire face were averaged by condition. Relative change in pupil dilation, normalized to each participant's average pupil size during preceding scrambled faces, was averaged for each trial as well as for each 250ms interval of each trial.

Results: Groups did not differ on overall time spent looking at the eyes, nose, mouth, or entire face. Furthermore, no group differences were observed for average pupillary response for any of the conditions. However, groups showed unique patterns of pupillary responses over the course of the 3-second stimuli presentation. Controls showed a dramatic increase in pupil dilation in the first 250ms followed by a sharp decrease in subsequent intervals, whereas individuals with ASD and their unaffected siblings showed a flat pupil response across the course of the trial. For all conditions, controls had significantly larger pupillary responses in the first 250ms interval than both individuals with ASD and siblings, $ps < .05$.

Conclusions: This study shows that, relative to controls, individuals with ASD and their siblings demonstrate divergent patterns of autonomic arousal in response to faces, though broad measures (e.g., average pupillary response, average looking time) may not capture these differences. In particular, these findings suggest that individuals with ASD and their siblings do not experience a typical initial increase in autonomic arousal when viewing faces. This lack of initial arousal may underpin reduced attention to social-emotional information, thus leading to downstream deficits in social understanding.

**160.125 125** Evaluation of the Common Genetic Architecture of Problematic Peer Relationships. B. St. Pourcain*[1], C. Haworth[2], O. Davis[3], K. Wang[4], N. J. Timpson[1], D. M. Evans[1], J. P. Kemp[1], S. M. Ring[1], W. L. McArdle[1], J. Golding[1], H. Hakonarson[5], R. Plomin[6] and G. Davey Smith[1], (1)*University of Bristol*, (2)*University of Warwick*, (3)*UCL*, (4)*University of Southern California*, (5)*Children's Hospital of Philadelphia*, (6)*KCL*

**Background:** Peer interaction plays an important role in the development of social competence, and problematic childhood peer

relationships often precede later maladjusted behaviour. Some links between early peer rejection and later maladaptive functioning however might be mediated through an underlying pathology. This includes impairments in social interaction skills, which are characteristic and heritable symptoms of the autistic dimension including Autism Spectrum disorders (ASD).

**Objectives:** Our study i) aimed to investigate genetic influences contributing to impaired peer relationships during childhood and adolescence, and ii) to identify population-based single SNP signals, which also contribute to risk for ASD.

**Methods:** Heritability was estimated using ≤7366 UK twin pairs (Twins Early Development Study, TEDS) with parent-report on peer problems at 4, 7, 9 and 11 years. A genome-wide analysis was conducted within N≤6000 children from a UK birth-cohort (Avon Longitudinal Study of Parents and children, ALSPAC) with parent-report on peer problems at 4, 7, 8, 10, 12, 13 and 17 years. Association signals were followed-up within independent children from TEDS (N≤2837) and were also investigated in the Autism Genetic Research Exchange (AGRE) sample (793 ASD pedigrees) and the Autism Case-Control cohort (ACC, 1204 ASD subjects, 6491 control subjects).

**Results:** Problematic peer relationships are substantially heritable throughout early/middle childhood ($h^2$=0.60-0.71). During this developmental period however, there might be only few measurable common additive genetic effects (DNA-based $h^2$≤0.12). During later adolescence by contrast the proportion of measurable common additive genetic effects is increasing (DNA-based $h^2$=0.14-0.27). Two population-based signals in ALSPAC (rs6451614 at 5p13.1 near *GHR*, $P_{17years}=9.6x10^{-6}$, rs7873232 at 9p24.2 near *GLIS3* and *RFX3*, $P_{13years}=7.3x10^{-6}$) were identified during later adolescence (out of 50 independent signals with $P<10^{-5}$ across all time-points) and showed evidence for replication in AGRE (rs6451614 P=0.00058, rs7873232 P=0.0030), but not the ACC (rs1858136, proxy for rs6451614, $r^2$=0.88, P=0.69; rs7873232 P=0.99). No comparable effect was observed within TEDS children spanning a younger age-range. Longitudinal modelling confirmed that genetic effects at both rs6451614 and rs7873232 varied across development, and that the underlying associations are complex.

**Conclusions:** Common genetic effects contribute to variation in problematic peer relationships, however the influence of measurable common additive genetic effect is strongest in later adolescence. Overlaps with the autistic continuum might be present, but many more samples might be required to reliably identify single associations.

**160.126 126** The Role of the X-Linked EFHC2 Gene in Social Cognition in Neurotypical Males. C. M. Startin*[1], C. R. Gibbard[1], C. A. Clark[1], M. de Haan[2] and D. H. Skuse[1], (1)*UCL Institute of Child Health*, (2)*University College London*

Background: Autism Spectrum Disorders (ASDs), which are characterised by impaired social cognition, occur more commonly in males than females. Reasons behind the sex difference of an increased male vulnerability to impaired social cognition are unknown, although genes on the X chromosome have been suggested to play a role as males possess one copy of this chromosome while females possess two. Further, women with Turner syndrome (TS, X-monosomy) also show impaired social cognition compared to typically developing women. Previous studies of X-linked influences on social cognition in women with TS have identified an influence of a single nucleotide polymorphism (SNP rs7055196) within the X-linked EFHC2 gene; women possessing the rare G allele showed poorer facial fear recognition than women possessing the common A allele.

Objectives: We investigated the influence of SNP rs7055196 on aspects of social cognition and related neural activity in neurotypical males to determine if this X-linked variation can help to account for the increased male vulnerability to impaired social cognition.

Methods: We compared neurotypical males possessing the A and G alleles at SNP rs7055196 on their facial fear recognition and theory of mind abilities, the face-selective N170 component (using event related potentials) and neural activity during a theory of mind task (using an fMRI paradigm).

Results: Males possessing the G allele showed poorer facial fear recognition accuracy compared to males possessing the A allele (P = 0.042, effect size = 0.214). Males possessing the G allele showed smaller N170 amplitudes in response to faces compared to males possessing the A allele (P = 0.028, effect size = 0.72). Males possessing

the G allele were less accurate at inferring others' mental states during the Reading the Mind in the Eyes task (a theory of mind task) (P = 0.045, effect size = 0.211), and showed reduced neural activity in the right superior temporal gyrus, left inferior parietal lobule and left cingulate gyrus during this task (P < 0.001 uncorrected) compared to males possessing the A allele.

Conclusions: The difference in fear recognition accuracy and N170 amplitude between the groups may be accounted for by males possessing the A allele using a more holistic/configural face processing mechanism than those possessing the G allele, as the N170 component is thought to be involved in holistic/configural face processing (i.e. processing faces as a whole). The group differences in theory of mind abilities and related brain activity may reflect higher empathising abilities in the males possessing the A allele, as activity in these regions has been linked to empathising. The effect sizes of these influences of SNP rs7055196 on social cognition were greater at the neural level compared to the behavioural level. Our results suggest an influence of SNP rs7055196 on social cognitive abilities in males. The location of this SNP on the X chromosome may contribute towards explaining the increased male vulnerability to impaired social cognition, helping to explain why males are more vulnerable to ASDs compared to females.

**160.127 127** Autistic Traits Modulate Self-Recognition in the Auditory Domain. A. Chakraborty* and B. Chakrabarti, *University of Reading*

Background: Atypical self processing is an emerging theme in autism research, suggested by lower self-reference-effect in memory, and atypical neural responses to visual representations of self face/body in individuals with autism. Most research onphysical self-processing in autism uses visual stimuli (e.g. self-face). However, the self is a multi-modal construct, and therefore it is essential to test self-recognition in other sensory modalities such as the auditory modality. Self recognition in the auditory domain remains relatively unexplored, and has not been tested in relation to autism and related traits.

Objectives: To develop a metric of auditory self recognition, we created a series of morphs of self-voice with other voices. We then tested if autistic traits modulated this metric of auditory self recognition.

Methods: In the first session 31 neurotypical adults (7 Males) participants' voices were recorded as they uttered a train of mono syllables /ba/. The individual participant's voice was then preprocessed and morphed with two unfamiliar ('other') voices, creating a continuum of morphs. In the second session, normally a few days later, participants performed a 'self-voice' identification task, classifying each morph as 'self' voice or an 'other' voice. A total of 88 morphed voice stimuli were presented, from 100% self to 0% self, in steps of 10%. All participants also completed the Autism Spectrum Quotient (AQ) online. 'Self-Voice' responses for each participant at each morph level were computed and a response curve was generated. The Area Under Curve (AuC) was computed for each participant which represented the area between the maximum self response (maximum stimuli recognised as belonging to self) to minimum self response (minimum stimuli labelled as belonging to self), and was used as a metric of the extent of auditory self recognition (i.e. the higher the AuC, the poorer the discrimination between self and other).

Results:

Individuals were able to recognize self voice from a single syllable utterance which contained no semantic information. However we found there are individual differences in judging the shift from self voice to other voice as indicated by the different morph levels at which this shift occurs. (Mean 27.5±15).

Crucially, the metric of auditory self-recognition as represented by the AuC for self-voice recognition was negatively correlated to the AQ scores (r= -.395, p=0.014).

There was no significant difference betweenthe two different unfamiliar voices on overall judgment of self vs other.

Conclusions: Our data shows individuals with higher autistic traits were better able to discriminate self from other voices. This may be due to the fact that our 'self-voice' stimuli represented the most basic voice utterance without any semantic content. This observation could arise due to both a) enhanced perceptual processing of auditory stimuli (as suggested by (Bonnel et al, 2003)and (Järvinen-Pasley et al, 2008)), as well as b) a narrower extent of self-

other overlap in individuals with Autism (Uddin et al., 2008).

**160.128 128** Comparing Social Cognitive Profiles of Autism and Schizophrenia. N. J. Sasson*[1], A. E. Pinkham[2], D. J. Faso[1], C. Simpson[2] and S. Kelsven[2], (1)*University of Texas at Dallas*, (2)*Southern Methodist University*

Background: Autism Spectrum Disorder (ASD) and Schizophrenia (SCZ) are categorically distinct conditions that debilitate functioning and quality of life. Recent genetic, behavioral and neuroimaging data suggest substantial overlap in the social cognitive phenotypes in the two disorders, yet no study to date has systematically examined social cognitive profiles in ASD and SCZ to elucidate patterns of similarity and distinction. Applications of social cognitive treatments developed in SCZ to individuals with ASD show limited efficacy, suggesting critical differences in social cognitive deficits across disorders. Delineating these patterns within matched samples on a common set of standardized tasks is imperative for identifying areas of convergence and divergence that can inform treatment efforts optimized for each disorder.

Objectives: To examine common and distinct features of social cognition in ASD and SCZ, and assess the relative contribution of general cognition to these profiles.

Methods: One hundred adults (46 SCZ, 40 typically developing controls, and 14 ASD) completed tasks of face perception (Benton Test of Facial Recognition), emotion recogntion (Penn Emotion Recognition Task; the ER40) and theory of mind (Cartoon Theory of Mind task; the CToM). We also obtained an estimate of general cognitive ability (the verbal section of The Wide Range Achievement Test), on which the groups did not differ.

Results: The ASD and SCZ groups performed worse than controls on the Benton face task ($F(2,98)=6.12$, $p=.003$, $h^2=.113$) and the ER40 ($F(2,99)=9.18$, $p<.001$, $h^2=.159$), and a trend emerged for the ASD and control groups to outperform the SCZ group on the CTOM, with no difference occurring between the ASD and control groups ($F(2,99)=2.01$, $p=.14$, $h^2=.40$). Direct comparison of ASD and SCZ revealed that the ASD group performed significantly better on the CTOM ($d=0.51$), while the SCZ group outperformed the ASD group on the Benton face task ($d=0.54$) and the ER40 ($d=0.42$). For SCZ, general cognitive ability was significantly correlated with each of our three social cognitive tasks: Benton ($r=.38$), ER40 ($r=.51$), CTOM ($r=.53$). For ASD, however, general cognitive ability did not correlate even minimally with the Benton ($r=.01$) or the CTOM ($r=-.04$) and non-significantly with the ER40 ($r=.38$).

Conclusions: Although both the ASD and SCZ groups generally performed worse than controls across all social cognitive tasks, they differed relative to each other on specific social cognitive abilities. Social cognition may therefore be comprised of distinct components that are differentially affected in ASD and SCZ. Additionally, because estimated IQ was associated with social cognitive performance for the SCZ but not the ASD group, cognitive functioning may contribute to social cognitive impariment in SCZ to a larger degree than in ASD. These distinct patterns of social cognitive deficit suggest that unique factors contribute to social dysfunction in ASD and SCZ, a finding that may help explain why individuals with ASD have derived limited benefit from social cognitive treatments developed for SCZ. Future remediation efforts may demonstrate improved efficacy by addressing disorder-specific areas of impairment. More data from participants with ASD are currently being collected, and will be included in analyses presented at the conference.

**160.129 129** Perceived Credibility of Witnesses with Autism Spectrum Disorder: Do Behavioural Manifestations Influence Mock Juror Perceptions?. K. L. Maras*[1] and A. Memon[2], (1)*University of Bath*, (2)*Royal Holloway*

Background:

People with autism spectrum disorder (ASD) may be over represented in the Criminal Justice System and victims, witnesses or suspects. They also exhibit a number of behaviours that are likely to affect their perceived credibility. For example, previous work suggests that jurors rely on non-verbal behaviours such as eye contact and body language when making judgments about a witness' credibility.

Objectives:

The first aim of this study was to examine whether witnesses with ASD are perceived as less credible than witnesses without ASD, irrespective

of the actual accuracy of their account. The second aim was to examine whether mock jurors' credibility ratings of ASD witnesses improved if they were aware of their ASD diagnosis and the behavioural manifestations of the disorder. According to the discounting principle (Kelley, 1972), explanations of behaviour are discounted if people are presented with a plausible alterative.

Methods:

Mock jurors (n = 125) rated videos of 36 witness participants with and without ASD recalling an eyewitness event. Half of the juror participants were informed that some of the witnesses had ASD and were briefly educated regarding behavioural features of ASD. The other half of jurors received no ASD information.

Results:

Overall, ASD witnesses were rated as less credible than witnesses without ASD in terms of competence and honesty, but did not differ in how confident they appeared. Some support was obtained for the prediction that ASD credibility ratings would be improved if jurors were aware of their diagnosis and able to attribute atypical behaviours to the ASD rather than view them as indicative of dishonesty and incompetence.

Conclusions:

Findings indicate that witnesses with ASD are perceived as being less credible than witnesses without the disorder. There may be a need for guidance to be given to judges, juries and magistrates regarding the emphasis they place on stereotyped ASD behaviours when arriving at judgements of credibility. Findings also have implications for areas in which it is important that observers are not inaccurately biased in their credibility judgements of people with ASD. This includes wider criminal justice settings such as parole board decisions and sentencing, as well other areas such as healthcare and risk assessments.

**160.130 130** Broader Autism Phenotype Characteristics and Social Adjustment in College Students: Mediating Effects of Depression. H. Gordon*[1], J. Waldron[1], A. Scarpa[1], S. W. White[2] and M. Benson[1], (1)*Virginia Tech*, (2)*Virginia Polytechnic Institute and State University*

Background: The Broader Autism Phenotype (BAP) is characterized behaviorally by subclinical symptoms and personality traits associated with Autism Spectrum Disorder (ASD). BAP characteristics include aloofness, rigidity, and pragmatic language difficulties (Piven et al., 1997; Landa et al., 1992). Historically, BAP characteristics have been studied in relatives of individuals with ASD; however, studies have shown that BAP characteristics are present in non-clinical samples (Baron-Cohen et al., 2001; Jobe & Williams-White, 2007; Wainer, Ingersoll, &Hopwood, 2011). While depression has been linked to mothers of children with ASD there are mixed findings regarding the relation between depression and BAP characteristics. Some studies (Micali et al., 2004; Piven & Palmar, 1999) have found that that depression is not associated with BAP traits specifically. However, Ingersoll, Meyer, and Becker (2011) found that presence of BAP characteristics uniquely predicted number of depressive symptoms in mothers of children with ASD, over and above parenting stress and severity of the child's autism symptoms. Additionally, Kunihira and colleagues (2006) demonstrated that BAP characteristics are correlated with both anxiety and depression.Research with college samples indicates that college students that exhibit BAP traits have fewer friendships and increased loneliness (Jobe & Williams-White, 2007) as well as deficits in social skills and social cognition (Sasson, Nowlin, & Pinkham, 2013). Affective disorders, such as depression and anxiety, are associated with both BAP traits and difficulties with social functioning. More research is needed to study how depression and anxiety affect the relation between BAP traits and social adjustment in college.

Objectives: This study sought to determine whether depression, stress and/or anxiety mediated the relation between BAP traits and social adjustment in college. Gender moderation was also explored.

Methods: A predominantly female sample ($N$ = 423, 75.1% female), ages 17-34 ($M$ = 20.30, $SD$= 1.91) was recruited from an undergraduate student population at a public mid-Atlantic university. The final sample (n = 333) included those participants with complete data on self-reported BAP (The Broader Autism Phenotype Questionnaire; Hurley et al., 2007), college social adjustment (Student Adaptation to College Questionnaire; Baker & Siryk, 1989), and

depression, anxiety, and stress (Depression Anxiety Stress Scales; DASS; Lovibond & Lovibond, 1985). Mediation was tested using hierarchical regression analysis and bootstrapped estimation of confidence intervals around the indirect effect (PROCESS; Hayes, 2013).

Results: Mediational analyses were run for DASS Total score, and depression, anxiety, and stress subscales individually, as mediators between BAP and college social adjustment. As predicted, BAP characteristics predicted poorer social adjustment in college (total effect = B = -7.891, SE =.897, $p$<.001). This effect was significantly and uniquely mediated by depression, controlling for anxiety and stress (indirect effect B= -1.336, Boot SE = .458, 95% CI=-2.291 to -.499). Gender did not moderate this effect.

Conclusions: Depression appears to play a powerful unique role in mediating the relation between BAP traits and social adjustment in college, above and beyond the effects of anxiety and stress. Limitations, and clinical implications are explored.

**160.131 131** Delineating the Nature, Severity and Frequency of Face Processing Abnormalities in Autism Spectrum Disorders. E. Loth*[1], E. Stolyarchuk[2], A. Duff[2], F. G. Happe[2] and B. Duchaine[3], (1)*Institute of Psychiatry*, (2)*Institute of Psychiatry, King's College London*, (3)*Dartmouth College*

Background:

Given the pivotal role of face processing in modulating social-communication, face processing deficits in ASD are increasingly viewed as potential "intermediate phenotypes" or "cognitive risk factors". However, previous studies have reported mixed results. From a treatment/ intervention perspective, a better understanding of the nature, frequency and severity of deficits of face processing abnormalities is still needed. Moreover, identification of underpinning factors is vital in order to inform interventions that go beyond the effort to increase performance levels and will instead target abnormalities in the underlying processes themselves.

Objectives:

(1) To systematically test whether people with ASD have deficits in different stages and aspects of face processing, including face detection, face perception, face memory, gender recognition, basic and complex emotion recognition, as well as object recognition.

(2) To investigate whether face memory could be improved by altering (or "normalising") the way people with ASD encode faces. Typically developing adults readily make social judgements when viewing novel faces ("is he nice or nasty?"). We hypothesised that in ASD this spontaneous tendency may be reduced and contributes to face memory deficits. Therefore, the explicit instruction to rate the trustworthiness of novel faces was predicted to increase face memory specifically in the ASD group.

Methods:

40 adults with ASD and 20 typically developing adults matched on sex, age and IQ completed a battery of computerised face processing tests. The battery comprised tests of face detection, the Cambridge Face Perception Task (CFPT), The Cambridge Face Memory Task (CFMT), a gender morph task, the Fleeting Films task, perceptual tests of happy/ angry emotion expressions, and a simple object recognition task. A modified version of the CFMT was created in which participants were asked to rate the trustworthiness of novel male faces during the encoding stage.

Results:

The ASD group showed significant impairments across all three stages of face processing (face detection p=.012, face perception, p=.008, face memory p=.0001), as well as in recognizing complex "fleeting" emotions from faces (p <.000001). Impairments were also found in recognizing two of three object categories but not in basic emotion perception (angry and happy faces) or gender matching ( all p >.08) .

Analyses of individual scores revealed that deficits were most frequent and profound on the fleeting films task with 89% of people with ASD performing below 2 SDs of the TD control group mean. Furthermore, severity of deficits were dimensionally correlated with autistic symptoms (r = -.44, p=.003). 36.8% of adults with ASD also showed strong deficits in face memory ( < 2SDs) and 68% had moderately-strong deficits (between 1-2 SDs). In addition, the trustworthiness-rating instruction yielded significantly improved face memory in both the ASD and TD groups.

Conclusions:

Using sensitive tests, people with ASD showed significant deficits across all stages of face processing and profound impairments in recognizing fleeting emotions. While improvements in face memory after the trustworthiness manipulation were not specific to the ASD group, our findings indicate the potential usefulness of interventions that emphasise social judgments during face encoding.

**160.132 132** Exploring the Developmental Social Profile of Females with ASD. R. Jamison*[1], J. Schuttler[1] and L. Edwards[2], (1)*University of Kansas Medical Center*, (2)*Unversity of Kansas Medical Center*

Background:

ASD prevalence rates rose 63% among females from 2002-2008 resulting in a marked increase in adolescents and young women with ASD today. However, studying girls with ASD remains a gap area (IACC, 2010) and many studies preferentially enroll males, who, due to a 4:1 increased prevalence, dominate the participant pool for research. We need more information about the heterogeneity of biological and behavioral features of ASD in females to determine whether the course of ASD is similar and if current interventions are appropriate for females (Koenig &Tsatsanis, 2005; Rivet & Matson, 2011). Some findings suggest boys are more socially impaired during childhood while girls are more impaired in adolescence (McLennan, Lord, & Schopler, 1993), which may be related to the increased complexity of social norms and expectations during adolescence (McLennan, Lord, & Schopler, 1993) and gender differences in interpersonal relationships. Continuing to study primarily male participants limits our understanding about ASD and the generalization of findings. *Our work addresses this critical barrier to progress in the field by targeting adolescent females with ASD.*

Objectives:

Our objective is to identify the developmental social profile of females with ASD in relation to their typically developing peers. We explore the similarities and differences in the social profile of adolescent females with without ASD, critical points in female social development necessitating further investigation, and the feasibility of conducting our protocol with an expanded age range sample.

Methods:

We employ qualitative research methods (Maxwell, 2005; Creswell, 2007) to explore the phenomenon of the social experience of females with ASD in relation to their peers. Participants include adolescent females (ages 14-19 years old) with and without ASD and their parents, resulting in four participant groups. Focus groups occur in waves, followed by analysis, and additional waves of groups in order to establish "saturation" (Charmaz, 2006) of a grounded theory of the social experience of adolescent females with and without ASD. We record, transcribe, and analyze each transcript for emerging codes (basic ideas) that come directly from the transcripts using microanalysis, with themes (reoccurring broader concepts) developing as they are identified and synthesized (Corbin & Strauss, 2008).

Results:

Findings indicate both similarities and differences for adolescent females with and without ASD in terms of their social activities and interests, friendships, self-perception, and perspectives and procedures for self-care. A preliminary model illustrates as females progress, social norms and expectations become complex, with expectations for increased independence and reliance on peers and decreased support from families and friends. This becomes more challenging for girls with ASD, who rely significantly more on family members to coordinate and facilitate social interactions and help with self-care.

Conclusions:

We hypothesize, based on our findings, that "barriers" are the social norms and expectations at critical points, which results in greater social difficulties and a widening "gap" in the social experiences of girls with and without ASD. Understanding the social experiences of females with ASD from a developmental perspective informs social competence interventions, including what, how, and when interventions may be the most effective.

**160.133 133** Dynamics of Social Movement Coordination As a Pathway to Understanding ASD-Specific Social Deficits. P. Fitzpatrick*[1], V. Romero[2], J. L. Amaral[2], C. L. Thomas[3], A. W.

Duncan[4], H. Barnard[4], M. J. Richardson[2] and R. C. Schmidt[5], (1)*Assumption College*, (2)*University of Cincinnati*, (3)*Cincinnati Children's Hospital*, (4)*Cincinnati Children's Hospital Medical Center*, (5)*College of the Holy Cross*

Background: The processes underlying the social deficits of individuals with Autism Spectrum Disorder (ASD) are not fully understood. When human beings interact with others, we implicitly coordinate our bodies and this has been found to facilitate interpersonal connections (e.g., Lakin & Chartrand, 2003). It is possible that such social movement coordination may be an important key for increasing understanding of ASD-specific social deficits (Fitzpatrick et al., 2013). Research that provides finer grained measures of mechanisms underlying social deficits in ASD may help elucidate the contradictory research and shed light on how it is that individuals with ASD can have very real problems in naturalistic social situations even though they are able to successfully perform social experimental tasks (e.g., Klin, 2000).

Objectives: This research evaluates whether fine-grained dynamical social movement coordination measures can provide insight into understanding ASD-specific social deficits. In particular, we tested whether dynamical measures of social movement coordination differentiate those with ASD, whether those differences were due solely to motor control problems, and explored the relationship between social movement measures and clinical assessments of social skill.

Methods: 47 typically developing children and 35 age-matched children with autism ($M$ = 101.34; $SD$ = 16.85, *Range* 72 -131 months) completed a series of clinical assessments and social cognitive tasks (theory of mind (ToM), joint attention, cooperation tasks). Social movement coordination was evaluated through an imitation and synchrony battery as well as an interpersonal game of pat-a-cake. Motor coordination was measured during in-phase and anti-phase drumming. The movements of the participants and the experimenter were recorded with a Polhemus and the time-series underwent cross-spectral coherence analysis to measure the correlation between the two time-series and the degree of co-occurrence of the interpersonal movements.

Results: Children with ASD had significantly lower coherence scores than TD children in imitation and synchrony ($p$ < .001) and pat-a-cake ($p$ = .003). In addition, coherence was lower for imitation than synchrony ($p$ < .001) for both groups. Children with ASD had lower coherence scores during drumming ($p$ < .001) and coherence was lower for anti-phase than in-phase drumming ($p$ < .001). Significant group differences were found on some social cognitive measures (responding to joint attention, visual perspective taking, behavioral interruption) but not others (ToM, behavioral reenactment, or initiating joint attention). There were significant correlations between social movement coordination and VABS social domain, and CBCL attention, social problems, and thought problems. Social movement coordination was not correlated with in-phase or anti-phase drumming.

Conclusions: Our findings suggest that children with ASD have difficulty synchronizing their movements with another person. Although children with ASD also exhibited poorer motor coordination, the social movement problems do not appear to be simply a motor control deficit as these measures were not related. Social movement measures were related, however, to clinical assessments of social deficits. While coordinating ones movements with another person typically helps to facilitate social connection, these findings suggest that children with ASD have disruptions in social movement coordination that may interfere with the formation of social bonds.

**160.134 134** Plasma Vasopressin Concentrations Predict CSF Vasopressin Concentrations in Human Neonates and Are Associated with Social Functioning in Children with Autism. D. S. Carson*[1], C. L. Howerton[1], J. P. Garner[1], R. A. Libove[1], S. A. Hyde[1], J. M. Phillips[1], A. A. Penn[2], A. Y. Hardan[1] and K. J. Parker[1], (1)*Stanford University School of Medicine*, (2)*Children's National Medical Center*

**Background:** The neuropeptide arginine vasopressin (AVP) has been linked to a variety of physiological processes, and more recently, to complex psychological processes including human social cognition. Several studies have outlined the potential for utilizing plasma AVP concentrations as a biomarker of disease status in neuropsychiatric disorders, including autism. Plasma AVP concentrations as a biomarker of social functioning are most meaningful if they are associated with brain AVP activity. The relationship between central and peripheral nervous system AVP activity, however, is not well understood. Given the growing interest in the role

of AVP in neurodevelopmental disorders, there is an urgent need to clarify the relationship between cerebrospinal fluid (CSF) and plasma AVP concentrations in young children and test whether AVP is a biomarker of social functioning in children with and without autism.

**Objectives:** The study objectives were two-fold: 1) to test whether plasma AVP concentrations predicted CSF AVP concentrations in human neonates; and, 2) to test whether plasma AVP concentrations predicted social functioning in a large cohort of children with autism, their unaffected siblings, and neurotypical controls.

**Methods:** Experiment 1: Participants were seventeen human neonates undergoing clinically indicated sepsis evaluation for standard risk factors. Within 72 h of birth, and at the time of clinically indicated lumbar puncture, CSF was collected using standard sterile procedures and whole blood was drawn into chilled, EDTA-treated vacutainer tubes. AVP concentrations were quantified in CSF and plasma using a commercially available enzyme immunoassay kit (Enzo Life Sciences, Inc., Farmingdale, NY). Experiment 2: Participants were seventy-nine children with autism, 52 unaffected siblings, and 62 neurotypical control children between the ages of 3 to 12 years. Autism diagnosis was based on the Autism Diagnostic Observation Schedule, Autism Diagnostic Interview Revised, and expert clinical opinion. Social phenotyping was conducted using the NEPSY-II Social and Perception Domain. Blood was collected from all participants and plasma samples were quantified using the AVP enzyme immunoassay.

**Results:** Experiment 1: Plasma AVP concentrations significantly and positively predicted CSF AVP concentrations in human neonates ($p<0.01$). Experiment 2: Plasma AVP levels *did not* differ by group or gender. An interaction effect was noted whereby plasma AVP concentrations significantly and positively predicted Theory of Mind in autistic children but not in non-autistic children ($p=0.023$).

**Conclusions:** These findings suggest that measurement of AVP in plasma samples might be a valid tool for inferential assessment of brain AVP activity, at least in pediatric populations. Further, our findings suggest that impairments in AVP signaling may be a biomarker of social impairments in children with autism, and that AVP biology may be a promising therapeutic target for enhancing social functioning in children with autism.

**160.135 135** Randomized Control Trials for Social Skills Interventions: Exploring the Initial Results for the SCI-a Program. J. P. Stichter*, M. Herzog and K. Bellesheim, *University of Missouri*

Background: Autism has been identified as a national health crisis. Social skills deficits are key signifiers of autism and manifest in varying severity across the spectrum. There is a paucity of well-designed research examining social skills interventions that utilize a package of research-supported teaching strategies and phenotype-specific social programming for those with High Functioning Autism (HFA). The Social Competence Intervention for Adolescents (SCI-A) utilizes evidence-based practices to target phenotype-specific skills associated with the social competence of individuals with HFA. Six years of development, including IES Goal 2 funding, has demonstrated the feasibility and acceptability of SCI-A for delivery to this group of students within school settings. Moreover, data indicates the promise of SCI-A in improving a variety of student social skills and behavioral outcomes.

Objectives: The current proposal shares the results of year one of a 5 year Goal 3 IES funded cluster-randomized trial (CRT) to examine the efficacy of SCI-A on student social, behavioral and classroom functioning as compared to Business as Usual (BAU) practices across twelve middle schools.

Methods: As part of the CRT design, half of the classroom teachers were trained and delivered the complete intervention during school programming to middle school students in groups of 4- 6. Assessment batteries were conducted with all students (n = 57) and one general educator per student about two weeks before (T1) and after (T2) the treatment students received intervention. Batteries included student performance on executive function (DKEFS, SPSI-R), theory of mind (NEPSY-II), and facial expression/emotion recognition tasks (NEPSY-II), and teacher reports of student social (SRS-2) and executive functioning (BRIEF) behaviors in the classroom.

Results: Random-effects ANCOVA models were used to analyze between-group differences (SCI

vs BAU) on each outcome assessment. SCI students' theory of mind improved from T1 to T2, and the improvement was greater than that of BAU students. Increased affect recognition was not found in either group. The SCI group evidenced greater increases in their reported rational problem solving than BAU. Results were mixed for SCI vs BAU comparisons on EF performance. Teachers reported improvements in SCI students' social and EF behaviors, and these improvements were greater than that of BAU students. ANCOVA results and effect sizes will be presented. Fidelity measures on teacher implementation indicate high levels of treatment integrity.

Conclusions: Congruent with six years of prior research on the Social Competence Intervention, the results of the present cluster-randomized trial indicated potential gains in execute functioning, rational problem solving, and social behavior for students with deficits in social skills who undergo the SCI-A. With the promise of future analyses anticipating 3-4 times more participants, SCI outcome measures will cut across categorical diagnoses, targeting phenotype-specific effects and informing teachers and clinicians alike of personalized treatment plans. Future research will determine the efficaciousness of SCI-A at 6-month follow-up. Furthermore, the implications and importance of CRT in applied settings by practitioners for social skills interventions will be explored.

**160.136 136** Early Predictors of Emotional Knowledge and Expression in Autism Spectrum Disorders. H. Gould*[1] and C. Kasari[2], (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

**Background:**

Many studies have documented the importance of emotional knowledge for later social competence in typical children (e.g., Denham, 1986; Dunn & Cutting, 1999; Schultz, Izard, Ackerman, & Youngstrom, 2001). However, less is known about the factors that lead to the development of these skills, or the growth trajectories of these skills in children with an autism spectrum disorder (ASD).

**Objectives:**

The aims of this longitudinal study were: (1) to examine the specificity and uniqueness of emotional knowledge and expression in autism spectrum disorders, and (2) to identify if joint attention skills in early development are predictive of greater emotional knowledge and increased positive reported expression of emotions at an older age.

**Methods:**

The initial sample consisted of 135 children: 37 with a diagnosis of an autism spectrum disorder, 66 with Down syndrome, and 32 with other developmental delays. At entry children were rated on initiations and responses to joint attention at a mean age of 3.17 years. The ASD sample was primarily Caucasian (65%) and male (84%) with a mean mental age of 24.81 months. At follow-up, 122 of the original children were assessed again, at a mean age of 10.7 years, on emotional labeling, identification, expression, and empathy.

**Results:**

The ASD group had a lower rate of responding to joint attention at entry ($p<.02$). Follow-up ANOVAs were used to compare the three groups on the emotional knowledge and expression measures and no significant differences were found between the ASD group and the other two diagnostic groups. A regression analysis found that early initiations of nonverbal joint attention gestures at entry predicted greater parent reported positive emotional expression ($p<.03$), holding diagnostic groups constant with a coefficient of determination equal to .224.

**Conclusions:**

These results suggest that improvements in joint attention at a young age may have long-term consequences for later expressive affect in children with ASD and other developmental disabilities. These data are consistent with other research that has found concurrent associations between joint attention and positive affect (Kasari et al., 1990) and increases in positive affect due to joint attention training (Lawton & Kasari, 2012).

**160.137 137** Oxytocin Increases Processing Efficiency of Socially Salient Visual Information. R. Tillman*[1], I. Gordon[1], J. F. Leckman[1], R. Feldman[2], A. Naples[1], G. Righi[1], K. A. Pelphrey[1] and J. McPartland[1], (1)*Yale University*, (2)*Bar-Ilan University*

Background: The social motivation hypothesis suggests that social dysfunction in ASD, such as

deficits in face processing, derive from atypical processing of socially rewarding stimuli. The neuropeptide oxytocin plays a key role in social behavior and is hypothesized to modulate the dopaminergic reward pathway during social interaction. Functional neuroimaging in healthy adults suggests that intranasally administered oxytocin enhances activity in brain regions involved in face processing; however, the modulatory influences of individual differences and context are poorly understood. Likewise, scant research has applied temporally sensitive imaging methods to examine the impact of oxytocin on face perception with regard to time course and stages of processing. For example, it is not understood whether oxytocin preferentially affects allocation of attention to relevant facial features or emotion decoding.

Objectives: The current study used event-related potentials (ERPs) to investigate the temporal dynamics of oxytocin's influence on the neural substrates of face perception. In addition, the relationships between autistic and anxious traits on the impact of oxytocin during face perception were evaluated. We predicted that oxytocin would significantly reduce latency of ERP components associated with face perception and that these reductions would be modulated by stimuli characteristics and individual traits.

Methods: Twenty-one typically developing adults completed two EEG recordings on two separate days in a double-blind, placebo-controlled within-subject design. Trait anxiety and autistic traits were measured using the State-Trait Anxiety Inventory (STAI) and the Social Responsiveness Scale (Adult Self-Report, SRS-A-SR). ERPs were recorded during administration of two experimental paradigms. In Experiment 1, neutral face and fearful face stimuli were presented in random sequence. In Experiment 2, grayscale digital images of neutral faces were presented while point of gaze was manipulated by preceding fixation points directing attention to the eyes, nose, or mouth. An ERP index of face perception (N170) was extracted for neutral and fearful faces in Experiment 1 and for each facial region in Experiment 2. In addition, an index of oxytocin sensitivity was calculated by computing N170 latency difference scores between conditions and oxytocin and placebo visits.

Results: In Experiment 1, N170 latency was significantly shorter to fearful faces only for subjects who had inhaled oxytocin ($p$=0.039). In Experiment 2, a main effect of condition indicated shorter N170 latency to the eye region compared the mouth and middle face regions ($p$=0.002). In the right hemisphere, N170 latency was significantly shorter to the eyes for subjects who had inhaled oxytocin ($p$=0.028). Self-reported anxiety ($p$=0.012) and lower self-reported social responsiveness ($p$=0.036) were significantly associated with sensitivity to oxytocin (i.e., individuals with higher anxiety displayed shorter N170 latency and individuals with lower SRS showed shorter N170 latency).

Conclusions: Intranasal administration of oxytocin resulted in increased processing efficiency of socially relevant information in terms of both facial affect and eye gaze. These effects were most pronounced in individuals with higher levels of autistic and anxious traits. Results emphasize the importance of applying temporally sensitive imaging methods to examine treatment-associated changes in processing efficiency and add to evidence supporting the potential utility of oxytocin to ameliorate autistic symptomatology.

**160.138 138** The "Face Deficit" in Visual Attention: Parsing Heterogeneity in ASD. J. Parish-Morris*[1], C. Chevallier[2], A. de Marchena[3] and R. T. Schultz[1], (1)*University of Pennsylvania*, (2)*Center for Autism Research, The Children's Hospital of Philadelphia*, (3)*The Children's Hospital of Philadelphia*

**Background:** As early as 6 months of age, children later diagnosed with ASD prioritize social information differently than typically developing children. Early atypical attention to people, in particular, is hypothesized to lead to downstream effects on social cognition that cause significant impairment in everyday social interaction. Visual attention to faces has recently been measured using infrared eye-tracking technology, and while the preponderance of evidence suggests reduced attention to faces in the ASD population versus typically developing controls (TDC), many studies have been hindered by small sample sizes that do not allow for adequate power to explore covariates that might shed light on the mechanisms responsible for these differences. The present study fills this gap by exploring visual attention to faces and objects in a sample of 372 carefully phenotyped children with ASD and TDC.

**Objectives:** Parse heterogeneity in visual attention to faces in a large sample of children with ASD and TDC, with the goal of explaining variance associated with reduced attention in the ASD group.

**Methods:** Children with ASD (N=252) and typically developing controls (N=120) watched 3 16-second sets of 4 video clips, 1 in each quadrant of a 32-inch screen, while their gaze data was collected at a rate of 60 Hz using a Tobii X120 system. Each set of videos included 2 neutral faces and 2 objects in action (e.g., car racing down a highway). Total fixation duration to faces relative to faces+objects was calculated for each participant, and this proportion was correlated with phenotypic variables hypothesized to explain individual variance.

**Results:** Consistent with the extant literature, children with ASD looked proportionately less at faces than TDCs, $F(1,370)=5.55$, $p=.02$. In the ASD group alone (but not the TDC group), more looking to faces was associated with higher scores on the Benton Test of Face Recognition ($r=.16$, $p=.02$), higher scores on the ADHD subscale of the Child and Adolescent Symptom Inventory (CASI; $r=.14$, $p=.03$), and lower overall scores on the Vineland Adaptive Behavior Scales (VABS; $r=-.12$, $p=.05$). Looking to faces was not associated with age, IQ, scores on the Social Responsiveness Scale, the Repetitive Behavior Scale, CASI social phobia or anxiety subscores, the VABS socialization or communication subscores, or the Brief shift score. In-depth analyses are ongoing, and will include sets of conceptually related scales (e.g., Benton and *Let's Face It!*) from which latent variables can be extracted and used to predict variance in attention to faces.

**Conclusions:** Atypical attention to social stimuli is one of the most robust findings in autism research, and was replicated in the present study comparing large samples of children with ASD and typically developing controls. Within the ASD group, a number of variables were found to correlate with individual differences in gaze to faces, including face processing skill and a measure of adaptive behavior. Planned analyses will model the unique and shared contributions of each of these individual variables to differences reflected at the group level.

**160.139 139** Emotional Prosody Processing in Behavior and Brain Function: Insights from Autism Spectrum Disorder. G.

Rosenblau*[1], D. Kliemann[2], I. Dziobek[2] and H. R. Heekeren[2], (1)*Yale University*, (2)*Freie Universitaet Berlin*

Background:

Social communication crucially depends on efficient processing of subtle nonverbal cues such as the emotional tone of voice, i.e., prosody. Social emotions convey important information about the speaker's attitudes and intentions (Burnett et al., 2011), thus understanding social emotional prosody is particularly important for successful social interactions. Although impairments in social communication have been consistently identified as a core feature of Autism Spectrum Disorder (ASD) (e.g., Tager-Flusberg, 1981), specific impairments in emotional prosody processing of individuals with ASD remain an under-researched topic with inconclusive results.

Objectives:

In this study, we investigated emotional prosody processing in adult individuals with ASD and healthy controls with newly developed behavioral and functional magnetic resonance imaging (fMRI) tasks. To increase ecological validity of the tasks and thus their sensitivity to the social impairments of individuals with ASD (e.g. Volkmar et al., 2004), the audio stimuli comprised a variety of social emotions (e.g., jealousy), different speakers, as well as implicit and explicit task conditions.

Methods:

Twenty-seven individuals with ASD and control participants (N=22), matched for age, gender and intelligence level, performed the new behavioral prosody recognition task. In this task participants listened to semantically neutral sentences that contained emotional prosody, whereby the majority of items comprised social emotions. Subsequently, participants were asked to label the emotional prosody from four different options. In a separate session, a sample of 20 ASD participants and 21 matched controls, largely overlapping with the initial behavioral sample, performed the emotional prosody fMRI task. In this task participants were presented with semantically neutral audios spoken with emotional or neutral prosody and had to either indicate the speaker's gender (implicit condition) or the correct emotion label from two options (explicit condition). Audios with emotional prosody covered

six basic and six social emotions, matched for valence and arousal levels as determined by pre-ratings.

Results:

Compared to controls, individuals with ASD were slower and less accurate at recognizing social emotions in the behavioral task (RT: t (1, 47) = -2.23, p = 0.03; accuracy: t (1, 41) = 2.72, p = 0.006). On the brain level, emotional prosody processing recruited a fronto-temporal network including the superior temporal sulcus (STS) and the inferior frontal gyrus (IFG) bilaterally in both groups. Importantly, the functional coupling between the right STS and right IFG was significantly reduced for emotional versus neutral prosody in individuals with ASD. When processing social versus basic emotions, individuals with ASD recruited the amygdala and STS to a lesser extent compared to controls and the functional connectivity between these regions was significantly reduced in the ASD group. Activity of core prosody regions such as the bilateral STS and IFG predicted accurate emotion recognition of social emotions on the behavioral task to a greater extent in controls than in individuals with ASD.

Conclusions:

In sum, these results provide evidence for dysfunctional emotional prosody processing in individuals with ASD on the behavioral and neural level and highlight the crucial role of the relationship between behavior and brain function and for unimpaired social functioning.

**160.140 140** Evaluating the Classification Potential of Eye-Tracking Measures Based on Perception of Social and Physical Contingencies in Toddlers with ASD. A. Abraham*[1], A. Trubanova[2], J. B. Northrup[3], D. Lin[4], P. Lewis[1], A. Klin[1], W. Jones[1] and G. Ramsay[5], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Virginia Polytechnic Institute and State University*, (3)*University of Pittsburgh*, (4)*Department of Neurology, Massachusetts General Hospital*, (5)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: Previous studies of two-year-olds with ASD demonstrated increased orientation to physical contingencies, in the form of audiovisual synchrony between sound and light, relative to social contingencies, in the form of faces and voices, which are preferentially attended to by typically developing (TD) peers. Further analysis showed that ASD toddlers were as sensitive to audiovisual synchrony as their TD controls. However, when social contingencies were introduced, TD toddlers differed in their preferential viewing pattern compared to ASD toddlers. When presenting naturalistic video stimuli of a caregiver and a moving object synchronized to the caregiver's speech, ASD toddlers were more distracted by the synchronous object than their TD counterparts.

Objectives: The goal of this study is to understand how physical and social contingencies bias attention in ASD and TD toddlers, and to evaluate the potential of eye-tracking measures of behavioral responses to social and physical contingencies as biomarkers for discriminating between toddlers with ASD and TD peers.

Methods: TD (N=22) and ASD (N=30) toddlers (Mean ± S.D: 23.3 ± 7.3 months) participated in a preferential looking paradigm, presenting audiovisual stimuli that varied in social context – circles, mouth-like ellipses and faces paired with tones or speech – to calibrate the biasing effect of social context and audiovisual synchrony on visual attention. To investigate generalization to naturalistic settings, a second cohort of TD (N=23) and ASD (N=44) toddlers (23.5 ± 6.1 months) were presented with videos showing a caregiver and a moving toy synchronized with the caregiver's speech against a playroom background. Eye-tracking measures of relative visual fixation on face, object, and background were collected and used to derive optimal classifiers for discriminating ASD from TD participants. Performance was evaluated by constructing Receiver Operating Characteristics (ROC) and calculating the sensitivity, specificity, and area under the curve (AUC) with cross-validation.

Results: When infants were presented with split-screen audiovisual stimuli consisting of caregiver faces and circles synchronized to the caregiver's speech, percentage of total fixation time spent on faces was significantly higher (P<.001) for TD controls (79.8 ± 21.2%) relative to ASD peers (56.2 ± 30.3%). Using this measure to classify TD and ASD toddlers yielded an ROC with sensitivity 71%, specificity 72%, and AUC = 0.78. When presented with naturalistic stimuli, percentage of

total fixation time spent on objects was significantly higher (P<.001) for ASD toddlers (34.1 ± 23.9%) compared to TD peers (17.9 ± 19.3%). Using this measure yielded an ROC with sensitivity 79%, specificity 79%, and AUC = 0.86.

Conclusions: Visual scanning patterns of toddlers with ASD are biased by the presence of social and physical contingencies in ways that differentiate them from their TD peers, to the extent that eye-tracking measures of visual fixation can successfully discriminate between diagnostic groups. In naturalistic settings, the presence of physical contingencies draws ASD toddlers' attention away from relevant social context, suggesting a mechanism of derailment of normative developmental processes of learning.

**160.141 141** Exploring the Social and Academic Engagement of Included Children with ASD. E. Rotheram-Fuller*[1] and J. J. Locke[2], (1)*Arizona State University*, (2)*University of Pennsylvania*

Background: In inclusion classroom settings, children with Autism Spectrum Disorders (ASD) typically show improvements in their social interactions, and the ability to generalize learned social skills (Carr & Darcy, 1990; Harrower & Dunlap, 2001). However, inclusion alone does not predict reciprocal social relationships (Orsmond, Krauss, & Seltzer, 2004). High-functioning children with ASD are more often neglected and rejected by peers, have poorer quality friendships, and experience more loneliness (Bauminger & Kasari, 2000; Kasari et al., 2012; Ochs, Kremer Sadlik, Solomon, & Sirota, 2001; Rotheram-Fuller et al., 2010).

Objectives: The current study seeks to determine classroom variables that may facilitate the development of meaningful social relationships for children with ASD in inclusion classroom settings.

Methods: This study was conducted in 11 urban public schools and included 52 students with ASD and 659 peers. All students in each classroom completed a social network survey to identify the friendships within each class (Cairns & Cairns, 1994). In addition, both classroom (n=15) and playground observations (n=28) were completed on students with ASD, examining teacher praise and behavioral correction, classroom structure, and social involvement with peers.

Results: Preliminary results suggest that children with ASD were significantly less socially involved with their classmates than their typically developing peers (p<.001). Playground observations confirmed these low levels of social involvement. Classroom observations showed that students with ASD were on task an average of 71.8% of observations, and performed better (stayed on-task) in classrooms when receiving more praise than corrective feedback.

Conclusions: It is important to explore both the academic and social repercussions of inclusion for students with ASD. Given difficulties in placement decisions, it is important to identify those factors of general education classrooms that may best support a child with ASD in both of these areas. Students with ASD may need more praise to stay on-task during instruction. However, more classroom characteristics may need to be explored in order to improve full social inclusion.

**160.142 142** Studying Social Attention in Autism Spectrum Disorders: Stimulus Type Matters. A. McVey*[1], R. T. Schultz[2], J. Parish-Morris[2], K. Rump[1], J. Pandey[3] and C. Chevallier[1], (1)*Center for Autism Research, The Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*, (3)*The Children's Hospital of Philadelphia*

**Background:** Autism spectrum disorders (ASD) are characterized by social and communication deficits, which we have hypothesized to be caused by atypicalities in the areas of social attention and responsiveness to social reward. Prior studies show that individuals with ASD attend to faces less than typically developing controls (TDCs), a pattern that is often coupled with an unusually high interest in certain non-social objects (e.g., trains). Infrared eye tracking technology has proven to be an effective method for examining social perception and social preferences in ASD, but different paradigms are more or less successful in revealing social attention deficits. We hypothesize that the nature of social stimuli shown in an eye tracking study has an impact on participants' gaze patterns, and that highly ecological, dynamic stimuli are optimal to uncover meaningful group differences in social attention.

**Objectives:** Compare the effectiveness of 3 different eye tracking tasks in distinguishing ASD and TDC participants on the basis of visual attention to face and object stimuli. The three tasks differed primarily on the ecological validity of the social stimuli: Static vs. Dynamic vs.

Interacting faces. This variation in ecological relevance enabled us to investigate patterns of attention modulation across social and nonsocial stimuli within and between TDC and ASD groups.

**Methods:** 66 children with an ASD (mean age = 11.78 years) and 22 TD children (mean age = 14.9 years) participated in three passive viewing tasks while eye gaze data was collected using a Tobii X120 system. The first task, a "Static Visual Exploration" task, showed still images of objects and people; the second, a "Dynamic Visual Exploration" task, simultaneously showed four dynamic video clips of individual faces and objects; the third, an "Interactive Visual Exploration" task, showed video clips of children playing.

**Results:** A repeated measures ANOVA was constructed to determine whether patterns of eye gaze to social vs. non-social stimuli of interest vary by diagnostic group and by task. A three-way interaction was found between Task (Static, Dynamic, Interactive), Stimulus-Category (social, non-social), and Diagnostic Group (ASD, TDC). Post hoc two-way ANOVAs within each task revealed that the Group by Stimulus-Category interaction was not significant for the Static task, reached trend levels for the Dynamic task, and was highly significant in the Interactive task.

**Conclusions:** Eye tracking is an increasingly popular method for evaluating visual behavior across multiple fields of study, including research in autism spectrum disorders. It is important to note, however, that not all eye tracking paradigms provide equally good metrics of social attention in ASD. Dynamic stimuli appear to be better than static images for measuring social response, and highly ecological paradigms (depicting actual interactive scenes) appear to be optimal.

**160.143 143** Cortisol Stress Response Patterns and Social Behaviors in Adolescent Boys with Fragile X Syndrome and Autism. S. McGrath*[1], J. Klusek[1], E. Schworer[1], J. Gunther[2], L. Abbeduto[2] and J. E. Roberts[1], (1)*University of South Carolina*, (2)*University of California Davis M.I.N.D. Institute*

Background: Fragile X syndrome (FXS) is the most common known single-gene cause of autism spectrum disorder (ASD) and is characterized by problems modulating social and emotional behaviors, particularly during stress. The hypothalamus-pituitary-adrenal axis (HPAA) measures stress response systems through secretion of cortisol (Foley & Kirshcbaum, 2010). Elevated and suppressed HPAA responses are correlated to shyness, social withdrawal, social anxiety and ASD in FXS (Roberts et al., 2009). These behaviors are also prevalent in individuals with idiopathic ASD; however, direct between-group comparisons of physiological patterns are needed to assess similarities and differences in symptomology.

Objectives: This study compared the relationship between cortisol indices of stress and avoidance, gaze and behavioral problems in boys with idiopathic ASD and boys with FXS which may inform targets for interventions. It was hypothesized that elevated cortisol would relate to increased social/emotional problems in both groups, with FXS displaying stronger trends.

Methods: This sample represents preliminary data from a larger ongoing study. Participants included boys with idiopathic ASD ($n$=7) and FXS ($n$=14). The FXS group was comparable ($M$=18.9, $SD$=2.4) in age to the ASD group ($M$=18.5, $SD$=2.4). The Social Approach Scale, a direct assessment measure, evaluated approach and avoidance behaviors on a 4-point Likert scale at pre-assessment and during the last hour of assessments. The Child Behavior Checklist, a parent-report instrument, assessed anxiety, withdrawn behaviors, externalizing problems, and overall behavioral problems. Cortisol was measured in two conditions: baseline and reactivity post-assessment. Change scores were computed as reactivity minus baseline. Cortisol was analyzed by radioimmoassay and values were natural-log transformed for normality.

Results: Greater cortisol change was significantly associated with decreased internalizing behavior scores ($r$=.81) and moderately related to decreased problem ($r$=.72), anxiety ($r$=.72) and externalizing behavioral scores ($r$=.69) in the ASD group. In contrast, no relationships were found between change scores and these behaviors in the FXS group. Baseline cortisol was significantly associated with increased internalizing ($r$=.76) and problem behavior scores ($r$=.73) in the ASD group. No other relationships between cortisol and behaviors were observed within FXS and ASD.

Conclusions: Contrary to our hypothesis, the ASD group demonstrated stronger relationships between cortisol change scores and overall

behavioral problems and internalizing and externalizing behaviors. This tentative finding suggests that individuals with ASD are modulating stress better as demonstrated by greater cortisol change predicting decreased problem behaviors. Greater cortisol change may be an adaptive response thus having a positive effect on social emotional behaviors in the ASD group. However, these data are initial findings from a subsample which will be expanded ($n$=60) by the time of the conference to permit more extensive analyses taking into account developmental characteristics that differ between the two disorders (e.g., IQ) and including analyses with a three group comparison: idiopathic ASD, FXS without ASD, and FXS+ASD.

References:

Foley, P., & Kirschbaum, C. (2010). Human hypothalamus-pituitary- adrenal axis responses to acute psychosocial stress in laboratory settings. Neuroscience and Biobehavioral Reviews, 35, 91-96.

**160.144 144** Examining the Roles of Affective Theory of Mind and Social Problem-Solving in the Expression of Depressive Symptomology in High-Functioning Autistic Adults and the Broader Autism Phenotype. S. L. Jackson* and B. Dritschel, *University of St Andrews*

***Background:*** Elevated rates of depression have been reported in High-Functioning Autism Spectrum Disorders (HFASD) populations. Two recent studies have found social problem-solving deficits to play the role of a significant partial-mediator between high autistic trait (AT) expression and elevated levels of depressed mood in neurotypical adults. Unfortunately, of these two studies, the only one that reported detailed results regarding the subscale relationships of the measured variables had a limited sample size. Furthermore, as neither study included a clinical sample, the implications for HFASD populations are unclear.

***Objectives:*** This study aims to confirm and expand upon these findings by examining: (i) will the subscale relationships previously detailed remain with the use of a larger sample size; (ii) will the mediating role of social problem-solving exist with the inclusion of a clinical (HFASD) sample; (iii) what role, if any, does the ability to recognize the feelings/emotions of others (affective Theory of Mind; aToM), a common area of deficit in HFASD populations, play in the relationships between these variables.

***Methods:*** This study will consist of 175 university/college students, divided into three groups: Group 1 (HFASD) will be comprised of 25 adults with HFASD; Group 2 (High AT) will consist of 25 neurotypical participants who are identified as reporting elevated AT levels (mean +1 SD); and Group 3 (Control) will consist of 125 neurotypical participants. All participants will be assessed on AT expression (Autism-Spectrum Quotient), depressive symptomology (Beck's Depression Inventory–II) social problem-solving abilities (Social Problem-Solving Inventory–Revised, and Means Ends Problem-Solving test), and aToM (Reading the Mind in the Eyes Test-Revised).

***Results:*** Preliminary results (n=135) produced findings confirming previous findings of higher AT expression being significantly associated with higher levels of depressive symptomology ($r=.36$, $p<.001$), deficits in social problem-solving ($r=-.30$, $p<.001$), and poorer aToM ($r=-.15$, $p<.05$). However, as no significant relationships were discovered between aToM and depressive symptomology or social problem-solving, this variable was not included in latter analyses (this issue will be readdressed once all data has been collected). The previously reported significant partial mediation was confirmed ($p<.05$), with social problem-solving ability accounting for 66.2% of the variance in depressive symptomology scores originally predicted by AT expression level. Assessment subscale analyses suggest that the specific social problem-solving deficits of assuming a negative orientation toward the problem and its outcome, producing less effective solutions when confronted with a problem, and a preference for avoiding confrontation of social conflict scenarios play key roles in the association between high AT expression and depressed mood. Between group analyses will be conducted at the completion of the study.

***Conclusions*** : Estimates suggest that roughly 37-43% of individuals with HFASD will suffer from depression at some point in their life. Determining social problem-solving's role in this phenomenon may provide proactive treatment options for depressive vulnerability in this population. Making use of the findings from this study, future

research should examine the efficacy of targeted therapies directed at the improvement of social problem-solving skills/attitudes in the treatment of depressed mood for individuals with HFASD and in the Broader Autism Phenotype.

**160.145 145** The Relationship Between Social Cognition and Social Functioning in Individuals with Autism Spectrum Disorder. L. Bishop-Fitzpatrick*[1], S. M. Eack[1] and N. J. Minshew[2], (1)*University of Pittsburgh*, (2)*University of Pittsburgh School of Medicine*

**Background:** Individuals with autism spectrum disorder (ASD) categorically experience marked challenges with social-cognitive and social functioning. Specifically, they have difficulty understanding the intentions, desires, and beliefs of others. They exhibit poor social awareness, social interaction skills, and adaptive behaviors. However, the association between social-cognitive and social functioning across the life course has not been adequately addressed. We hypothesize that social-cognitive functioning positively predicts social functioning, after controlling for demographic factors and intelligence.

**Objectives:** Examine the relationship between social cognition and social functioning composite scores in verbal individuals (n=130) with ASD and without intellectual disability.

**Methods:** Cross-sectional data were collected from 130 individuals with ASD who were participants in two separate studies conducted in the University of Pittsburgh's Center For Autism Research. The hypothesis was tested by creating standardized (z-metric) composite indices of social-cognitive and social functioning, based on theory of mind (Sally-Anne, John and Mary, and preference judgment tasks) and social functioning (the Social Responsiveness Scale, the Child Behavior Checklist, and the Vineland Adaptive Behavior Scales) measures, respectively. Average age was 11.8. Average Performance Intelligence quotient (PIQ) was 106. Males accounted for 90.0% (n=117) of the sample. A series of general linear models were constructed to predict social functioning from cognitive functioning, gender, age, and PIQ.

**Results:** As expected, results indicated that there was a significant prediction of social functioning by social-cognitive functioning, gender, age, and PIQ, $F(4,125)=3.790$, $p=.006$, $R^2=.108$, adjusted $R^2=.080$. Both social-cognitive functioning ($B=.200$, $t(125)=3.005$, $p=.003$, $sr^2=.065$) and age ($B=-.046$, $t(125)=-2.507$, $p=.013$, $sr^2=.045$) contributed significantly to the prediction of social functioning. There was no significant prediction of social functioning by gender ($B=.015$, $t(125)=.096$, $p=.923$, $sr^2=.000$) or PIQ ($B=.001$, $t(125)=.393$, $p=.695$, $sr^2=.001$).

**Conclusions:** Findings indicate that social cognition and age predict social functioning in individuals with ASD. These findings highlight the role of social cognition in social functioning. Results also indicate that younger participants with ASD function better socially which may reflect better intervention or conditions in which younger individuals have more structure and support for positive social functioning than adults. These results highlight the importance of a developmental perspective on the deficits that emerge in social cognition and social functioning as individuals with ASD age and cognitive demands associated with the social environment become more complex. The lack of difference in ability and function between males and females may reflect the comparable IQ and language levels of both genders participating in these research studies in contrast to studies of representative samples which may reveal that females with ASD are often more severely affected on average than males with ASD. These findings suggest the important impact of evolving community intervention programs, especially early interventions, and the considerable need to build interventions for adults with ASD which have been seriously neglected in the longstanding focus on "early" intervention. The lifelong plasticity of the brain and the far greater portion of life spent in adulthood support the need for an equal focus on intensive cognitive interventions for adults with ASD.

**160.146 146** Problem Behaviors of School-Age Children with and without Autism Spectrum Disorders during Mother-Child Play Tasks. T. A. Hassenfeldt* and A. Scarpa, *Virginia Tech*

Background: Dyadic synchrony, defined here as the mutual warmth and responsiveness between a mother and her child, is a largely unexplored construct in school-aged children, including those with Autism Spectrum Disorders (ASD). Dyadic synchrony helps a child regulate their behaviors, emotions, and cognitions, leading to improved self-regulation (Deater-Deckard, Atzaba-Poria, & Pike, 2004). We compared observed child

behaviors during play with their mothers, to parent-reported problem behaviors.

Objectives: We hypothesized that children with ASD would have worse behavior scores during play, due to their symptomatology. For both groups, we expected that low parent reports of problem behaviors would predict positive child behaviors during play.

Methods: Twenty-five 4-11 year-old boys and girls (M=7.24 years, SD=2.1 years; 88% Caucasian) participated along with their mothers. Ten children (100% male) met the clinical cut-off for ASD on the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000); 15 did not (40% male). Mother-child dyads completed nine play tasks adapted from the Marschak Interaction Method (The Theraplay Institute, 2005), such as playing with figurines, completing a puzzle, drawing, and sharing a snack. Mothers also completed survey measures (e.g., Parenting Stress Index, Short Form (PSI; Abidin, 2005); Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997); Aberrant Behaviors Checklist (ABC; Aman, Singh, Stewart, & Field, 1985)). Two trained coders, blind to group, independently coded videotapes using the Coding System for Mother-Child Interactions (Healey et al., 2010) to score child behaviors, mother behaviors, and overall dyadic synchrony. Total child behavior scores included three subscales: cooperation and compliance, enthusiasm, and negativity and hostility (reverse-scored).

Results: Group differences were found on the cooperation-compliance and enthusiasm subscales, as well as the total child score. No group difference was seen for the negativity and hostility subscale. Predictors of total child behavior score included Difficult Child score on the PSI, $b$=.69, $t(22)$=16.69, $p$<.05, peer problems on the SDQ, $b$=-.49, $t(22)$=-9.73, $p$<.05, emotional problems on the SDQ, $b$=.67, $t(22)$=7.97, $p$<.05, hyperactivity on the ABC, $b$=-.83, $t(22)$=-9.67, $p$<.05, and speech problems on the ABC, $b$=-.62, $t(22)$=-7.84, $p$<.05. Significant differences were found between the ASD group and the non-ASD group on all subscales listed above, $p$< .05-.001.

Conclusions: The ASD group showed less compliance and enthusiasm during the play tasks, and more negative behaviors reported by parents. Surprisingly, there was no group difference on observed negativity, indicating that "less positive" interactions were not necessarily "more negative." Hyperactivity and emotional problems may make a child less cooperative, enthusiastic, and focused during play with their parent. Parent perception of their child's problem behaviors also predicted the child's overall negative behaviors during those tasks, indicating a rather accurate perception of these behaviors. However, the relationships between child behaviors and speech and peer problems were slightly less clear. It remains to be seen whether this relationship was due to ASD symptoms, or a broader connection across groups, between speech and social abilities and play behaviors. Despite power limitations and a significant gender difference between groups, our findings suggest important future directions for exploring the characteristics of mother-child relationships in this population.

**160.147 147** Gaze Patterns in a Narrative Task with FMR1 Premutation Carriers and Autism Parents. N. Maltman*[1], R. S. Hoedemaker[2], P. C. Gordon[3] and M. C. Losh[1], (1)*Northwestern University*, (2)*University of North Carolina*, (3)*University of North Carolina-Chapel Hill*

Background:

Fragile X syndrome, caused by a mutation in the *FMR1* gene, is the most common inherited cause of intellectual disability and the most common monogenic disorder associated with autism. Carriers of the *FMR1* gene in its premutation have been shown to exhibit executive dysfunction, as well as elevated rates of certain personality and language features of the broad autism phenotype (BAP).

Objectives:

This study aims to further investigate potential similarities between carriers of the *FMR1*premutation and parents of individuals with autism by examining eye gaze patterns during a narrative elicitation task using illustrated narrative stimuli. We also examined whether BAP status impacted eye gaze patterns across groups.

Methods:

Participants included 56 parents (33 female, 23 male) of children with autism (ASD), 20 maternal carriers of the *FMR1* premutation (CX), and 24

parents (15 females, 9 males) of typically developing individuals (TD) with no family history of autism or fragile X. Features of the BAP were measured using direct assessment interviews coded blind to group status. On the eye tracking measure, participants were presented with six different emotionally evocative images from the Thematic Apperception Test, and gaze was recorded using the Tobii X60. Each slide was presented for eight seconds. After each image was removed, participants were instructed to tell a story about the picture they had just seen.

Results:

Fixation patterns differed across groups, and in relation to BAP features. On the visually complex images (i.e., involving multiple characters and extensive scenery), CX parents spent less time on faces ($F=5.20$, $p<.03$) and animate features ($F=26.01$,$p<.01$), and more time on inanimate features ($F=25.01$, $p<.01$) than control parents. However, the socially complex slides, (i.e. only two characters), showed variable patterns. ASD parents differed from controls across all fixation measures including proportion of time on interest areas ($F=104.00$, $p<.01$), faces ($F=19.50$, $p<.01$), animate features ($F=1.10$, $p<.01$), and inanimate features ($F=1.10$, $p<.01$). When considering BAP features, both ASD and CX parents with these characteristics made fewer fixations overall than those without BAP features ($F=143.86$, $p<.01$) and controls ($F=105.80$, $p<.01$). This group also spent more time on inanimate aspects of the slides (e.g., furniture, scenery) and less time on the most salient features of the slides (i.e.., main characters) than did participants without the BAP($F=28.39$,$p<.01$), or controls ($F=17.63$, $p<.01$).

Conclusions:

Overall, these data suggest that when processing complex scenes during narrative generation, both CX and ASD parents spend less time fixating on socially salient aspects of complex scenes than do controls, and also fixate less frequently. This suggests a bias away from social processes, particularly in BAP groups, which may be related to overall narrative quality, as initial exploratory analyses suggest. This study provides information on eye gaze patterns across typical, autism, and premutation groups, thus informing understanding on social processing through multiple modalities across related clinical groups.

**160.148 148** Siblings of Individuals with and without Autism Spectrum Disorder and Other Intellectual Disabilities. C. Shivers*, *Michigan State University*

Background: Research on siblings of individuals with intellectual and developmental disabilities (IDD) is a relatively small field, with roots in early qualitative studies. While many early studies did not distinguish outcomes based on the nature of the brother or sister's disability, more recent studies have focused on siblings of individuals with autism spectrum disorder (ASD).

Objectives: The present study compares behavior and functioning among individuals with autism spectrum disorder, typically-developing individuals (TD), and individuals with other intellectual and developmental disabilities (IDD), as well as emotional outcomes for siblings of these individuals.

Methods: Data was collected as part of a study comparing adolescent siblings of individuals with and without intellectual and developmental disabilities. The present study included a total of 49 families of adolescents with an IDD, 26 of whom had a child with an ASD diagnosis, and 48 families of typically-developing children. Families were eligible to complete the online survey if there were only two children, both of whom were between the ages of 12 and 18 and living at home. A parent completed measures of behavior, functioning, and impact on the family for the child with ASD/IDD (the "target child"), as well as a measure of parental optimism. The "sibling" (child without autism or IDD) completed self-report measures of empathy and emotionality toward the target child. Groups were then compared using chi-squares and ANOVAs.

Results: Target children in the ASD group had significantly more behavior problems ($F=15.77$, $p<.001$), negative impact on the family as a whole ($F=15.65$, $p<.001$), and negative impact on the sibling ($F=28.23$, $p<.001$) than target children in both the TD and IDD groups. Parents of children in the TD group reported less financial burden ($F=30.88$, $p<.001$) than parents of children in the ASD and IDD groups, as well as higher levels of target child functional abilities ($F = 49.35$, $p<.001$) while parents of children in the ASD group reported lower levels of optimism than

parents of children in the TD and IDD groups ($F=5.89$, $p<.01$). Siblings did not show any differences in empathy based on their brother/sister's disability, but siblings of children in the ASD and ID groups reported feeling more anxiety toward the target child than did siblings in the TD group ($F=10.36$, $p<.001$)

Conclusions: These analyses reveal fascinating patterns of target child behavior and sibling outcomes. Though target children in the ASD group had significantly more behavior problems than target children in the IDD group, siblings of children with ASD did not report any different outcomes than siblings in the IDD group. While previous research has found that target child behavior problems predict sibling outcomes, in the present study, behavior problems did not differentiate sibling emotionality. Additionally, while parents of children with ASD reported more negative impact on the sibling than parents of children in the IDD group, sibling self-report revealed no differences in outcomes between the two groups, highlighting the importance of multiple informants when studying siblings.

**160.149 149** Specific Events That Impact the Topography of Salience When Individuals with and without ASD View Naturalistic Social Scenes. E. M. Kim*[1], S. Shultz[2], W. Jones[3] and A. Klin[3], (1)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta, Emory University*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*

Background: Social interactions are dynamic events that unfold in real time and in complex environments. When faced with open-ended, fast-paced scenes, knowing both *what* is important to process and *when* something is important to process is critical for adaptive social action. Research from our laboratory has shown that typically-developing (TD) individuals are remarkably attuned to what is most relevant to process: during open-ended viewing of complex scenes, visual scanning of TD viewers converges on a common location during more than 80% of viewing time. By contrast, individuals with ASD encounter great difficulty when faced with open-ended social scenes, showing less attunement to socially relevant information as scene complexity increases. The current study expands on these results by examining how specific content within a social scene may guide or fail to guide visual scanning in a group of TD viewers and viewers with ASD.

Objectives: To examine how specific elements within naturalistic social scenes (e.g. vocalizations and facial expressions of varying affect) elicit or fail to elicit convergent visual scanning in TD adolescents and adolescents with ASD.

Methods: Adolescents with ASD (mean age = 16.67 (3.92) years; n = 21) and TD controls (mean age = 16.86 (4.5); n = 17) were matched on age and verbal function. Eye-tracking data were collected during viewing of video scenes depicting realistic social interactions. We used kernel density estimation to quantify the level of convergence of visual scanning at each moment in time for each group. The onset and offset of specific events (positive, negative, and neutral facial expressions and vocalizations) were coded on a frame-by-frame basis. Level of convergence in visual scanning corresponding to each coded event was examined for both groups.

Results: Preliminary analyses reveal higher visual convergence in visual scanning among TD viewers compared with ASD viewers across all categories of scene content. For TD viewers, results showed a significant effect of variation in affective content on levels of scanning convergence. For ASD viewers however, there was no significant effect of affective content on levels of convergence in visual scanning.

Conclusions: Variation in affective content is an important factor that affects the attention of TD adolescents when viewing scenes of dynamic social interactions. By contrast, the level of convergence in visual scanning among viewers with ASD is not significantly modulated by changes in affective content. Reduced modulation in visual scanning due to changes in affective content in ASD may be accompanied by increased attention to socially irrelevant distractors. Future research will utilize similar methods to identify unique aspects of scene content that drives convergence in visual scanning in ASD viewers.

**160.150 150** Multidimensional Assessment of Empathy in Children with ASD. L. K. Bryant*[1], K. Schauder[2] and C. Cascio[3], (1)*Vanderbilt University*, (2)*University of Rochester*, (3)*Vanderbilt University School of Medicine*

Background:

Successful social interaction requires the ability to recognize and interpret others' emotions. These skills are considered foundational for empathy, but research suggests that empathy is not a single construct. Cognitive empathy (CE), the capacity to infer others' mental states, is closely related to emotion recognition. Affective/emotional empathy (EE) is the observer's emotional response to another person's emotional state. Previous studies examining CE and EE in autism spectrum disorders (ASD) report impaired CE but intact EE (Rogers et al. 2007). Many previous studies of empathy used paradigms that individually measured either CE or EE and relied on direct self-report of EE**.** To address these concerns, Dziobek et al. (2008) developed the Multifaceted Empathy Test (MET). The paradigm was designed to measure CE and EE simultaneously, including both direct (sympathy) and indirect (arousal) measures. In this report, adults with ASD were impaired in CE, but not on EE, consistent with previous reports. However, there are no published reports utilizing this multidimensional paradigm in children with ASD.

Objectives:

We aimed to simultaneously measure CE and EE in children with ASD using a modified version of the MET, the Multifaceted Empathy Test-Juvenile (MET-J: Poustka et al., 2010), expecting to replicate previous findings in adults with ASD.

Methods:

19 children with ASD and 17 typically developing (TD) children, ages of 7-16, participated. Participants viewed photographs of people in emotionally charged situations and were asked to infer the person's emotion by choosing from a list of four adjectives (CE). As an indirect measure of EE, participants were asked to rate their arousal in response to each picture using a visual-analog scale (SAM; Lang et al. 1997). Feedback was given after all CE decisions in order to assure subsequent arousal judgments were based on the correct emotion. Lastly, as a direct measure of EE, participants rated how much they sympathized with the person in the picture, using a visual-analogue scale.

Results:

There were no significant differences between ASD and TD individuals on EE ($t(34) = 1.18$ , $p = .247$) or arousal ($t(34) = .79$ , $p = .437$). However, the groups differed on CE ($t(34) = 2.09$ , $p = .044$) , with lower accuracy in the ASD group. Additionally, there were significant positive correlations between arousal and EE (ASD, $r = .916$, $p < .001$ TD, $r = .801$, $p < .001$). CE and arousal were also negatively correlated in the ASD group ($r = -.619$, $p= .005$).

Conclusions:

Consistent with prior studies, children with ASD were less accurate at explicitly identifying emotions (CE) but demonstrated intact emotional empathy. Strong positive correlations between arousal and EE are consistent with the somatic marker hypothesis of emotion (Damasio et al.,1991). The ASD group's ability to correctly identify emotions (CE) decreased as arousal increased, suggesting a possible role of anxiety. The MET-J dissociated CE deficits from intact EE in this sample, confirming and extending previous findings in adults to children with ASD. Future directions include the use of physiological measures of arousal to validate the arousal ratings.

**160.151 151** The Relationship Between Neural Sensitivity to Social and Non-Social Positive and Negative Feedback and Autistic Traits. V. Carter Leno*, A. Naples, R. Tillman, H. S. Reuman, E. Levy, H. Rutherford, A. Cox and J. McPartland, *Yale University*

Background:

Individuals with autism spectrum disorders (ASD) have difficulties with interpersonal functioning. Prominent theories suggest this is due to social cues being less salient in individuals with ASD. Social cues can express both positive and negative feedback, therefore are important modifiers of behaviour. Thus, decreased sensitivity to these cues may underlie atypical development in ASD. With regard to positive feedback, research reports mixed findings, with some reporting a selective decreased neural response to positive social feedback in ASD, and others a more general impairment in the processing of positive feedback. Atypical neural response to social exclusion is seen in ASD, yet unimpaired neural response to monetary (non-social) feedback has been reported elsewhere. Specific comparison between sensitivity to

negative social and negative non-social feedback in ASD remains unexplored.

Objectives:

To determine whether sensitivity of neural response, as indexed by event-related potentials (ERPs) to 1) social and non-social positive feedback and 2) social and non-social negative feedback, is associated with self-reported autistic traits.

Methods:

35 typically developing individuals completed a measure of autistic traits using the Social Responsiveness Scale –Adult (SRS-A). ERPs were recorded with a 128 Channel HydroCel Geodesic Sensor Net whilst subjects completed a modified cued incentive go/no-go task. Feedback was provided by presentation of a pre-recorded video after completion of each trial block. *In Experiment 1 (positive feedback),* correct responses led to the presentation of three conditions of feedback: 1) Social (verbal encouragement by observer), 2) Non-social (gain of sweets) and 3) neutral (geometric shape). *In Experiment 2 (negative feedback),* incorrect responses led to the presentation of three conditions of feedback: 1) Social (verbal criticism by observer), 2) Non-social (loss of sweets) and 3) neutral (geometric shape). ERPs were time locked to in-task performance cues, those indexing motivational salience (feedback related negativity; FRN), and allocation of resources (P300) were extracted.

Results:

For *positive feedback (Experiment 1)*, repeated measures ANOVA found no overall effect of feedback type upon P300 amplitude ($F(2,70)=.39$, $p=.68$). In the social feedback condition, a significant negative relationship was found between level of autistic traits and P300 peak amplitude ($r(35)=-.35$, $p=0.04$). No significant relationship was found in the non-social feedback condition ($r(35)=-.08$, $p=.67$). For *negative feedback (Experiment 2), a*nalyses in progress examine amplitude and latency of FRN and P300 components using repeated measures ANOVA, with condition of feedback as the within-subjects factor (negative social, negative on-social, neutral).

Conclusions:

Our findings suggest less allocation of resources towards social stimuli in individuals with increased autistic traits. This is in line with the social motivation hypothesis, proposing a decrease in salience attributed to social stimuli in individuals with ASD underlies the behavioural phenotype. Results concerning negative feedback will elucidate whether the pattern of decreased sensitivity to social cues associated with autistic traits is selective to positive feedback, or extends to negative social feedback. Understanding where difficulties in feedback processing lie will prove useful in guiding targeted interventions in ASD.

**160.152 152** Proneness to Self-Conscious Emotions and Theory of Mind in Adults with Autism Spectrum Disorders. D. Davidson*, S. B. Vanegas and E. Hilvert, *Loyola University Chicago*

Background:

The ability to conceptualize, reflect upon and understand one's own emotions and the emotions of others is central to emotional competence. Some emotions, such as self-conscious emotions, are thought to require more cognitive self-reflection than others (Tracy & Robins, 2008). Moreover, self-conscious emotions facilitate our social interactions and relationships by motivating us to adhere to social norms as well as personal standards (Else-Quest et al., 2012). Although once thought to be disruptive, self-conscious emotions are now theorized to be fundamentally involved in the regulation of social behavior.

Objectives:

Despite the importance of self-conscious emotions (embarrassment, pride, guilt, shame), most studies explore basic emotion (e.g., fear) processing. The purpose of this research was to examine proneness to self-conscious emotions in adults with Autism Spectrum Disorders (ASD) with neurotypical adults. Given the potential links between self-conscious emotions and behavioral regulation, it is crucial to evaluate these relations in individuals with ASD.

Methods:

Adults with ASD and neurotypical adults were recruited through online listservs, including those providing services to adults with ASD. Currently, 30 neurotypical adults (NT-A), and 12 adults with ASD (ASD-A) have participated. All individuals completed the Social Responsiveness Scale-2

(SRS-2; Constantino, 2012). Measures assessing self-conscious emotions included the Test of Self-Conscious Affect (TOSCA; Tangney et al., 2002), and Embarrassment Scenarios (Sabini et al., 2001). Additional measures assessed Theory of Mind (Faux Pas Task; Stone, et al., 1998) and negative evaluation (Brief Fear of Negative Evaluation Scale; Leary, 1983). The online measures took approximately 45 minutes to complete.

Results:

Preliminary analyses demonstrated significant differences between adult groups. Assessments of shame were higher for adults with ASD on the TOSCA, $t(40) = -2.90$, $p = .006$, $M_{ASD\text{-}A} = 3.28$, $SD_{ASD\text{-}A} = 0.72$, $M_{NT\text{-}A} = 2.62$, $SD_{NT\text{-}A} = .65$, and on the Embarrassment Scenarios, $t(40) = -2.644$, $p = .012$, $M_{ASD\text{-}A} = 5.37$, $SD_{ASD\text{-}A} = 1.34$, $M_{NT\text{-}A} = 4.03$, $SD_{NT\text{-}A} = 1.53$. Additional differences between groups were found in fear of negative evaluation, $t(40) = -4.536$, $p < .001$, $M_{ASD\text{-}A} = 37.17$, $SD_{ASD\text{-}A} = 6.46$, $M_{NT\text{-}A} = 27.13$, $SD_{NT\text{-}A} = 6.48$. These differences could not be accounted for by differences in Theory of Mind, $t(36) = .81$, $p = .425$, $M_{ASD\text{-}A} = 34.92$, $SD_{ASD\text{-}A} = 6.72$, $M_{NT\text{-}A} = 36.35$, $SD_{NT\text{-}A} = 4.15$.

Conclusions:

Adults with ASD showed greater proneness to shame and embarrassment, and demonstrated more fear of negative evaluation, than neuroptypical adults. These findings are compelling, given that past research has found that adults with ASD show limitations in perceiving emotions (e.g., Boraston et al., 2007). The *experience* of emotion, however, may differ in individuals with ASD. For example, recent research has shown that individuals with ASD perceived subtle displays of emotion as being more intense than neurotypical individuals (Tell, Davidson & Camras, 2013). ToM abilities, however, did not underlie the present findings. We are currently exploring the origins of these findings.

**160.153 153** Social Anxiety and Social Reciprocity in Children and Adolescents with High Functioning Autism. L. V. Usher*[1], C. A. Burrows[1], C. B. Schwartz[2] and H. A. Henderson[1], (1)*University of Miami*, (2)*Yale Child Study Center*

**Background**: Social anxiety has been found to be negatively related to social skills in typically and atypically developing children (Erath et al., 2007). For children and adolescents with high functioning autism (HFA), anxiety may negatively impact the implementation of social skills, especially in a novel setting where anxiety is likely to be high. Although the majority of literature reveals a negative correlation between anxiety and social competence in autism (e.g., Chang et al., 2012), Bellini (2004) found a curvilinear association between self-reports of these variables, suggesting that moderate levels of social anxiety may support the successful application of social skills better than low or high levels of social anxiety.

**Objectives**: The goal of this study was to examine associations between observed social reciprocity in a laboratory task with an unfamiliar peer and parental reports of social anxiety in typically and atypically developing children and adolescents.

**Methods**: Participants with HFA ($N = 39$, 34 males, $M_{age} = 13.85$, $SD = 2.80$) were paired with unfamiliar comparison participants (COM; $N = 39$, 34 males, $M_{age} = 14.14$, $SD = 2.36$) on gender, age, and verbal IQ, and observed during an unstructured interaction. Eye contact, conversational efficacy, and appropriateness during two different tasks were coded from the videotaped interaction to index social reciprocity. Social anxiety was assessed using the parent-reported total score of the Social Anxiety Scale for Children-Revised (La Greca & Stone, 1993).

**Results**: Polynomial regression analyses were conducted separately for HFA and COM participants to examine whether the relation between social anxiety and social reciprocity was better modeled by a linear or nonlinear function.

For typically developing participants, there was a linear association between parent-reported social anxiety and observed social reciprocity, $F(4, 30) = 3.22$, $p = .03$. The quadratic and cubic regression models did not significantly improve the model, $p$s = .28 and .79, respectively.

For participants with HFA, the linear regression examining parent-reported social anxiety as a predictor of observed social reciprocity was not significant, $F(4, 31) = 1.83$, $p = .15$. The quadratic regression examining the addition of parent anxiety squared was significant, $F(5, 30) =$

3.17, $p$ = .02. Adding the squared term resulted in a significantly better model, β = -2.90, $t$ = -2.66, $p$ = .01, $R^2$ = .35, $R^2_{change}$ = .16, indicating that the association between social reciprocity and social anxiety was best represented as an inverted-U. Adding a cubic term did not result in a significantly better model than the quadratic, $p$ = .82.

**Conclusions**: As hypothesized, we found an inverse relation between parent-reported social anxiety and observed social reciprocity for comparison participants, but for participants with HFA, the relation between social anxiety and social reciprocity was represented as an inverted-U. For children with HFA, a moderate level of social anxiety may be beneficial. Future research would benefit from investigating these associations longitudinally to parse apart the order of effects.

**160.154 154** Social Engagement of Children with ASD in Inclusive Setting: The Role of the Social Profile of Typically Developing Peers. M. Zakai -Mashiach*[1], M. Al-Yagon[2] and E. Dromi[1], (1)*Tel Aviv University*, (2)*Tel-Aviv University*

Background: The present study focused on typically developing (TD) children's social interest in a child with Autistic Spectrum Disorder (ASD) who was included in their preschool class. Although the literature presents rich evidence on the importance of inclusion for children with ASD, only few studies have been conducted to date in terms of the factors that facilitate social interest of the TD children toward the included child with ASD.

Objectives: The main goal was to examine which social-emotional characteristics of the TD children influence their social interest toward the child with ASD. A secondary goal was to identify which factors in the inclusive environment may facilitate this natural interest, such as the attitudes of the preschool teacher and the functional profile of the child with ASD.

Methods: Sixteen preschool teachers from sixteen different preschool classes in Israel which included a child with ASD participated in this study. One hundred ninety-three TD preschoolers participated in the study. Data was collected from a questionnaire administered to the teachers, as well as from tasks conducted with the TD children. The Profile of Peer Relations (Walker, 2005) was administered in order to collect information on the social profile of the TD children. A questionnaire for the teachers about inclusion (My Thinking About Inclusion; Stoiber et al., 1998) was used to test beliefs and attitudes concerning inclusion. The Childhood Autism Scale (CARS; Schopler et al., 1988) was used to assess the presence and severity of symptoms of the child with ASD.

Results: Findings indicated the following: the pro-social behaviors of the TD children contributed the most to spontaneous social interest toward the ASD child; the teacher's degree of preparation to teach in inclusive classroom setting had an impact on the social interest of the TD children toward the ASD child; and finally, the abilities of the ASD child, especially non-verbal communication, social profile and sensitivity to sound and touch also explained the degree of social interest.

Conclusions: Findings from this study suggest the role of several factors that contributed to the social engagement of children with ASD in inclusive preschool settings. Thus, social-behavioral features of TD children and the degree of preparation of the teacher to teach in inclusive setting contributed to the opportunities to encourage social interaction among children with ASD and their TD peers. Therefore, it is important to support social engagement not only by means of specific intervention programs that are targeted towards increasing social skills in the included children with ASD, but also by fostering aspects in the natural educational environments that can increase the likelihood of social interaction between TD and children with ASD. By fostering a better understanding of inclusion among teachers and caregivers in general, and promoting social interaction between unequal partners in particular, the challenge of social inclusion can be more easily attainable.

**160.155 155** Trying to Make Sense of a Heterogeneous Disorder: A Factor Mixture Modelling Approach to Autism Spectrum Disorder. V. E. Brunsdon*[1], E. Colvert[2], P. F. Bolton[2] and F. Happe[2], (1)*SGDP, Institute of Psychiatry, King's College London*, (2)*King's College London*

Background: Autism spectrum disorder (ASD) is behaviourally defined by the presence of social and communication impairments and restricted and repetitive behaviours. The clinical phenotype is characterised by considerable heterogeneity, with individuals presenting with severe

impairments through to more subtle deficits. This heterogeneity is often considered as a hindrance in the study of the aetiology and genetics of ASD.

Objectives: (1) To identify homogeneous subgroups within ASD using a Factor Mixture Modelling (FMM) approach. (2) To explore the similarities/differences of individuals assigned to each subgroup in terms of age, gender, diagnosis, and their symptom and cognitive profiles.

Methods: Participants were drawn from a large population-based sample of adolescent twins. The sample consisted of 251 individuals (*M*=13.5, *SD*=0.68; 174 males). 137 participants had a diagnosis of ASD (*M*=13.51 years, *SD*=0.73; 118 males), 40 had a diagnosis of broad spectrum autism (*M*=13.40 years, *SD*=0.56; 30 males), and 72 were unaffected co-twins (*M*=13.49 years, *SD*=0.65; 26 males). All twin pairs were behaviourally assessed for ASD symptomatology using parent report (Autism Diagnostic Interview-Revised, ADI-R) and direct observation (Autism Diagnostic Observation Schedule-Generic, ADOS-G). All twin pairs were also administered an extensive cognitive battery to measure IQ, language ability, theory of mind ability, executive functioning, and central coherence. Analyses: FMM combines latent class analysis and confirmatory factor analysis to stratify individuals into relatively more homogeneous subgroups. Factor mixture models were tested using the raw subscale scores of the 37 items from the ADI-R. To guide the choice of the number of classes and factors for the FMMs, six latent class analyses (one-to-six classes) and three confirmatory factor analyses (one-to-three factors) were carried out. The fit of these models was assessed using goodness-of-fit criteria.

Results: Overall, a 'two-factor, five classes' FMM was chosen as the best fit of the data. According to this final FMM, individuals could be classified into five relatively homogeneous classes (C1: 23%, C2: 18%, C3: 17%, C4: 29%, C5: 13%, of the sample). A two factor solution fitted the data best; one factor corresponding to social/communication deficits, and a second factor corresponding to restricted and repetitive behaviour impairments. Age did not differ across the five classes. There were a higher proportion of females in C1 and C2, with a higher proportion of males in C3, C4, and C5. The proportion of ASD diagnosis differed across the five classes, with C5 comprising only of ASD diagnoses. IQ also differed across classes. Individuals assigned to C1 had the lowest social and communication impairments, with few restricted and repetitive behaviours. The severity of ASD symptoms significantly increased through C3 to C5, with individuals assigned to C5 showing the most severe impairments. However, the cognitive profile across the five classes was similar.

Conclusions: Five subgroups were identified using an FMM approach, which were largely based on symptom severity. Across the subgroups, individuals received different diagnoses, had a differing IQ profile, and a differing symptom profile. Age and cognitive profile was stable across subgroups. The findings also support the two symptom dimensions of ASD, as proposed in the DSM-5.

**160.156 156** Understanding Trajectories of Diurnal Rhythm of Cortisol in Children with Autism Based on Psychological and Behavioral Profiles. G. Han*, A. Tomarken and B. Corbett, *Vanderbilt University*

Background:

Individuals with autism spectrum disorders (ASD) are characterized by marked impairments in social interaction and communication, stereotypic repetitive behaviors, and difficulties responding to changes throughout the day. Furthermore, children with ASD also present significant heterogeneity in their profiles of stress responsivity. Previous studies investigating diurnal rhythm of cortisol have shown notable variability and dysregulation of cortisol throughout the day in children with ASD compared to typically developing (TYP) children. Moreover, findings suggest that sensory sensitivity may be a moderator of reactivity to daily stress, though few studies provide a comprehensive analysis of diurnal cortisol in children with ASDs.

Objectives:

The goal of this study was to replicate and extend previous findings in a new cohort of children to achieve a more detailed understanding of the heterogeneity of diurnal cortisol profiles of children with and without ASD. First, this study aimed to assess the stability of the diurnal cortisol profile in ASD and TYP children, and then sought to clarify the between- and within-group differences through consideration of time-of-day

differences, behavioral, and psychological factors as potential covariates of cortisol regulation.

Methods:

The study sample consisted of 64 unmedicated, prepubertal children between 7 and 12 years old, 36 with ASD and 28 typically developing children. Salivary cortisol was collected for three diurnal cycles, consisting of four samples per day (T1: waking, T2: 30-minutes post-waking, T3: afternoon, T4: 30-minutes before bedtime), for a total of 12 samples per child. All participants also completed a battery of neuropsychological tests, including measures of intelligence (IQ) and parent-report measures of sensory sensitivity, stress sensitivity, and adaptability to change. Data were analyzed using a piecewise linear mixed effects model with the cortisol awakening response (T2-T1) separated out from the linear decline of cortisol levels from the awakening response until the end of the day (T2 to T4).

Results:

Preliminary results indicate that the two groups differ in steepness of the linear decline from T2 (30-minutes post-waking) to T4 (30-minutes before bedtime), with individuals with ASD having a flattened slope compared to the TYP group and elevated evening cortisol. Furthermore, there is a dampening effect of peak cortisol and linear decline in the ASD group from Day 1 to Day 3. In this sample, age, IQ, and sex do not significantly affect diurnal cortisol trajectories. However, scores on sensory and stress sensitivity, time of awakening, and adaptability to change throughout the day (and their interactive effects) are still to be explored to help elucidate between- and within-group differences of diurnal rhythm.

Conclusions:

The findings support a growing body of literature emphasizing the identification of specific subgroups of children with ASD, such as those with increased sensory sensitivity, and how cortisol regulation is moderated in terms of differential individual profiles. The findings support a complex interplay between physiological and behavioral stress and sensory sensitivity.

## 161 Specific Interventions - Non-Pharmacologic

### 161.157 157 Disseminating an Evidence-Based ASD Intervention: Predictors of Community Providers' Likelihood of Implementation

N. I. Berger* and B. Ingersoll, *Michigan State University*

**Background:** Individuals with ASD often require intensive and specialized intervention, yet significant barriers, including insufficient provider training and support, have impeded their access to evidence-based services. Given the significant service-need discrepancy for this population (Sperry et al. 1999; Stahmer and Gist 2001), recent efforts have focused on developing and improving strategies for dissemination and implementation of evidence-based ASD intervention, particularly in community settings (Brookman-Fraze, Drahota, & Stadnick, 2011, Vismara, 2009). However, the extant research has largely focused on the extent to which community providers can be trained to successfully implement evidence-based treatments for ASD with fidelity. Factors directly influencing community providers' decision regarding whether or not to implement an evidence-based treatment for ASD are still largely unknown. This is important to consider given research indicating that implementation is affected by factors such as provider experience and sense of competence, organizational functioning, and perceived program barriers (Durlak & DuPre, 2008; Turner, Nicholson, & Sanders, 2011). Better understanding of these constructs as they pertain to community-based providers of ASD services would allow the field to more effectively train practitioners in evidence-based interventions and increase availability of evidence-based programming for this population.

**Objectives:** This study examined the training of community-based mental health providers in an evidence-based ASD parent training intervention (Project ImPACT), and their subsequent implementation of the program. We sought to assess the effect of training on participant knowledge of intervention techniques and likelihood of implementing the intervention post training. A secondary aim was to evaluate the extent to which participant demographics, participant characteristics, and potential barriers to implementation uniquely predict likelihood to implement the program following training.

**Methods:** Individuals attending community-based trainings in Project ImPACT (an evidence-based ASD parent training intervention) were invited to participate in the study. Those who consented to

participate completed surveys before the workshop and after completing training. Surveys assessed participant demographics, sense of competence, perceived acceptability of treatment, self-efficacy in implementation, barriers to treatment implementation, and likelihood of implementation.

**Results:** Community providers significantly increased their knowledge of intervention techniques and expressed a greater likelihood of implementing the intervention after receiving training in Project ImPACT. Correlational analyses indicated that level of education, mandatory attendance at training, general sense of competence, acceptability of treatment, and efficacy in ability to implement the intervention were all related to likelihood of implementing the evidence-based intervention by community members. Multiple hierarchical linear regression was used to evaluate the unique impact of these factors in predicting likelihood of implementing Project ImPACT. While demographic variables accounted for a significant amount of variance in implementation of the intervention, program acceptability emerged as a unique predictor of implementation over and above other variables entered into the model.

**Conclusions:** These results indicate that training influences community practitioners' understanding of and intent to use an evidence-based treatment for ASD. The perceived acceptability of the intervention is strongly associated with providers' reported likelihood of using the intervention. Results underscore the importance of designing and disseminating evidence-based treatments in a way that maximizes program acceptability for community practitioners.

**161.158 158** Treatment Effects of the Joint Attention, Symbolic Play, Engagement and Regulation (JASPER) Intervention for Toddlers with ASD. A. Gulsrud*[1], C. Kasari[2] and G. Hellemann[1], (1)*UCLA*, (2)*University of California Los Angeles*

**Background:** Behavioral interventions have well-established efficacy for children with autism spectrum disorders (ASD). Targeted approaches that focus on early core deficits in joint attention and play have led to lasting expressive language gains in preschoolers (Kasari et al., 2008, 2012). Far less is known about the efficacy of this targeted intervention for the youngest children with ASD and whether other-than highly trained interventionist can be effective in deploying the intervention.

**Objectives:** This study was developed to test a parent-mediated adaptation of the JASPER intervention for toddlers with ASD. JASPER is already an empirically supported treatment for preschoolers with autism (Kasari et al., 2006, 2008, 2012).

**Methods:** Participants were randomized to either a parent-mediated JASPER condition or an individualized psychoeducational intervention (PEI) targeting parental stress-reduction (Brereton and Tongue, 2006). Families met one-on-one weekly with a trained therapist for 10 weeks. 86 parent- child dyads were enrolled in the study. Children had an average chronological age of 31.5 months and mothers were on average 35.9 years old. The sample of toddlers consisted of mostly Caucasian males with an average IQ of 68.

**Results:** The main effect of interest was the interaction between time and treatment, testing if there are differences in the degree of change over time that is associated with the treatment condition. We chose either a poisson GLMM or a linear GLMM depending on which model fit the data better based on the BIC. Joint Engagement: The distribution of this variable was sufficiently close to normal to allow the use of a standard GLMM (AIC of the linear glmm=1964, AIC of the poisson glmm=4599). There was a significant group x time interaction ($F(1,84)=43.52$, $p<.01$), showing that there was a significant increase in the length of time spent in joint engagement for the JASPER treatment compared to the PEI condition. Number of Functional Play Types: Function play did not show zero inflation ($F(1,84)=0.25$, $p=.61$), but due to its skew it was modeled using a Poisson GLMM (AIC=694) over a Linear GLMM (AIC=789). There was a significant group by treatment interaction showing that the JASPER group increased more in their number of different types of functional play acts than the PEI group ($F(1,84)=6.56$, $p=.01$). Highest Play Level Achieved: This variable did not show significant zero inflation ($F(1,84)=0.39$,$p=.53$), but the skew of the data meant it was modeled more accurately using a Poisson distribution (AIC=833) than a normal distribution (AIC=839). Using the Poisson model, there was a significant treatment by time interaction for the highest play level achieved

(F(1,84)=9.13, p<.01), such that the JASPER group increased more than the PEI group.

**Conclusions:** This study highlights the efficacy of employing a parent-mediated approach to JASPER for toddlers with ASD. Increases in child outcomes were noted for the JASPER condition in the areas of joint engagement, diversity of functional play and the highest play level achieved compared to a psychoeducation intervention focused on parental stress reduction.

**161.159 159** A Systematic Review of Theory of Mind Based Interventions for Autism Spectrum Disorder. S. Fletcher-Watson*[1] and H. McConachie[2], (1)*University of Edinburgh*, (2)*Newcastle University*

Background: The 'Theory of Mind' model suggests that most people with autism spectrum disorder (ASD) have a profound difficulty understanding the minds of other people - their emotions, feelings, beliefs and thoughts. As an explanation for some of the characteristic behaviours of people with autism spectrum disorder (ASD), this model has had a significant influence on research and practice. It implies that successful interventions to teach ToM could in turn have far-reaching effects on behaviours and outcome.

Objectives: To review the efficacy of interventions based on the ToM model for individuals with ASD.

Methods: We searched 8 international databases including MEDLINE and PsycINFO, as well as performing hand searches of relevant journals, conference proceedings and making contact with authors in the field. Studies were selected on the basis that they reported on an intervention linked to ToM in one of four clearly-defined ways: designed to test the ToM model; designed to teach ToM; designed to teach precursor skills of ToM (e.g. emotion recognition, joint attention); based on or inspired by ToM models of autism. The replicability of these definitions was tested in a pilot by 3 naïve raters. In addition, included studies presented new randomised controlled trial data from participants with a confirmed ASD diagnosis. Studies were selected and data extracted by two researchers independently and a third expert arbitrated.

Results: Twenty-two randomized controlled trials were included in the review (n=695). Studies were highly variable in their country of origin, sample size, participant age, intervention delivery type, and outcome measures. Risk of bias was variable across categories. Further complexity in interpreting results was introduced by the wide range of measures used within each outcome category and by the mixed results from these measures. Studies were grouped into four main categories according to intervention target / primary outcome measure. These were: emotion recognition studies, joint attention and social communication studies, imitation studies, and studies teaching ToM itself. Meta-analyses indicated that interventions targeting emotion recognition had a positive effect on the target skill (mean increase of 0.66 points, z=3.19, p<.001) and that therapist-led joint attention interventions can promote production of more joint attention behaviours within adult-child interaction (mean increase of 0.55 points, z=2.45, p=.01). However there was also a lack of effect of intervention on joint attention initiations as measured using a standardised assessment tool (mean increase of 0.23 points, z=0.63, p=.53). No adverse effects were apparent.

Conclusions: While there is some evidence that ToM, or a precursor skill, can be taught to people with ASD, there is little evidence of maintenance of that skill, generalisation to other settings, or developmental effects on related skills. Furthermore, inconsistency in findings and measurement means that evidence has been graded of low quality and we cannot be confident that suggestions of positive effects will be sustained as high-quality evidence accumulates. Further longitudinal designs and larger samples are needed to help elucidate both the efficacy of ToM-linked interventions and the explanatory value of the ToM model itself.

**161.160 160** Click-East: Using Data Collected within a Therapeutic Ipad App to Elucidate Results of a Randomised Controlled Trial. S. Fletcher-Watson*[1], A. E. O'Hare[1], H. Pain[1] and H. McConachie[2], (1)*University of Edinburgh*, (2)*Newcastle University*

Background: Young children with diagnoses of 'core' autism regularly pay little attention to other people and often struggle to follow social cues. On the other hand, children with autism often have good technological skills and a preference for using technology in leisure and education. We also know that early intervention is crucial to have the maximum beneficial effect on outcome. These three issues come together in the application of

novel technologies to social difficulties of very young children.

Objectives: The Click-East research project designed and then evaluated an iPad app to teach the fundamentals of social attention to pre-schoolers with autism. In this report we explore how data collected by the app can elucidate the mixed results of an randomised controlled trial.

Methods: The app was developed using a multi-faceted participatory design, expert consultation and pilot testing process with children with ASD, parents, teachers, and other professionals. The completed app was evaluated in a rigorous randomised controlled trial (n=54) with intervention and waitlist control groups, membership stratified by autism severity using the *Autism Diagnostic Observation Schedule*. The primary outcome was based on a rating of child social and communication behaviours during parent-child play at 6 month follow-up. Other measures included the *MacArthur Communicative Development Inventory* (vocabulary and gesture), and the *Communication and Symbolic Behaviour Scales Caregiver Questionnaire.*

Results: There were no main effects of intervention at a group level on the primary outcome measure nor on other outcome measures of vocabulary, gesture, and communication and social behaviour. This was the case both immediately after intervention and at follow-up. However there was statistically-defined reliable individual change in 5/27 of the intervention group compared to 1/27 of the waitlist control group. An exploration of the demographic characteristics and baseline scores of intervention responders and non-responders revealed no systematic group differences. However, one strength of this technology-based intervention is the opportunity to use detailed data collected within the app to explore the patterns of game play across individuals.

Conclusions: We will consider our findings in the light of pragmatic approaches to education and support. The RCT evidence suggests that the intervention is at worst benign and at best may benefit a sub-set of children in social attention. The app has now been downloaded by 85,000 users meaning that the impact of even a small and minority beneficial effect could already have reached thousands. We also consider spin-off benefits for families (e.g. peer respect, increased on-task behaviour) and review the future of technology-based early intervention for autism.

**161.161 161** Creating Symptom Profiles to Anticipate Treatment Outcomes for Adolescents with ASD Following the UCLA PEERS® Intervention. J. Hopkins*[1], B. Schwartzman[2], S. Bates[3] and E. A. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience and Human Behavior*, (2)*UCLA*, (3)*Pepperdine University*

Background: Adolescents with autism spectrum disorder (ASD) present with unique symptom profiles and varying degrees of symptom severity with regard to social deficits. These deficits fueled the evolution of targeted social skills interventions addressing the core deficits seen in ASD (Rogers, 1998). One such example includes the Program for the Education and Enrichment of Relational Skills (PEERS®), an evidence-based, parent-assisted social skills intervention for adolescents with ASD without intellectual disabilities. Traditionally, targeted interventions like PEERS® have focused on classifying individuals with ASD according to IQ and/or diagnosis alone. Yet, few studies have examined the extent to which symptom profiles, rather than IQ or diagnosis, anticipate treatment outcome. Thus, classifying adolescents with ASD into symptom profiles may provide more useful insights into who is most likely to benefit from targeted interventions.

Objectives: The purpose of this study is to (1) identify distinct symptom profiles related to social functioning among adolescents with ASD, and (2) distinguish unique treatment outcomes across these symptom profiles following the PEERS® intervention.

Methods: Participants in this study included 139 adolescents with ASD from 11-18 years of age ($M$=14.17, $SD$=1.70) who presented for social skills treatment with their parents through the UCLA PEERS® Clinic. In order to create symptom profiles of social functioning, a *k-means* Cluster Analysis was performed using baseline parent-reports of social functioning on the subscales of the Social Responsiveness Scale (SRS; Constantino, 2005). Treatment outcome was assessed for self-esteem (PHS-2: Piers et al., 2002), anxiety (SAS; La Greca, 1998), empathy (EQ; Baron-Cohen, 2004), social skills and problem behaviors (SSIS; Gresham & Elliot, 2008), friendship quality (FQS; Bukowski, 1994),

peer engagement (QSQ; Frankel & Mintz, 2008), and social skills knowledge (TASSK; Laugeson & Frankel, 2010). One-way ANOVAs and independent T-tests were used to identify differences in treatment outcome across clusters (i.e., symptom profiles).

Results: Using a *k-means* Cluster Analysis, three distinct symptom profiles emerged across adolescents with ASD using the SRS: mild, moderate-to-severe, and severe impairments in social functioning. Significant differences across clusters were observed in relation to anxiety on the SAS [$F(2,104) = 7.04$, $p=.001$], social skills on the SSIS [$F(2,74) = 5.82$, $p=.004$], and overall empathy on the EQ [$F(2,26) = 4.09$, $p=.028$] in the areas of emotional reactivity [$F(2,26) = 3.54$, $p=.044$] and cognitive empathy [$F(2,26) = 4.30$, $p=.024$], according to parent reports following treatment. Significant differences in overall self-esteem on the PHS-2 were observed across clusters [$F(2,107) = 2.77$, $p=.05$], according to adolescent reports following treatment. While treatment gains were observed across all clusters in the following areas, there were no significant differences between clusters in empathic social abilities on the EQ, peer engagement on the QSQ, friendship quality on the FQS, or social skills knowledge on the TASSK.

Conclusions: The marked differences in treatment outcomes across symptom profiles among adolescents with ASD highlight the multi-faceted phenotypes observed on the spectrum, and emphasize the necessity to "go beyond" IQ and diagnosis alone in order to better understand who is more likely to benefit from targeted treatment intervention in this highly diverse population.

**161.162 162** A Teacher Instructing Caregivers of Toddlers with Autism Spectrum Disorder How to Spontaneously Increase Words. K. Lawton*, S. Barrett and L. Mong, *The Ohio State University Nisonger Center Early Childhood Education*

**Background:** Due to the increasingly younger age of average ASD diagnosis, there is tremendous opportunity to start intervening earlier and, thus, more dramatically improve a child's developmental trajectory. There is growing consensus that toddlers with ASD will experience more robust cascading long-term benefits if interventions are specifically focused on ameliorating core autism deficits. The vast majority of toddlers with an Autism Spectrum Disorder (ASD) receive community Part C Early Intervention (EI) services, however these EI services rarely focus on core ASD deficits.

**Objectives:** This study investigated the effectiveness of a classroom teacher instructing caregivers of toddlers with ASD how to improve a central ASD impairment, the production of spontaneous words. The manualized intervention was tailored to the unique needs of each toddler with ASD and was specifically focused on improving the quantity of child spontaneous single words. The study was concerned with determining if this increase occurred immediately after the intervention concluded and at a one-month follow-up visit. Secondary goals were to determine if child social communication skills of joint attention and requesting gestures improved as a result of the intervention and whether the intervention was favorably perceived.

**Methods:** A multiple-baseline across participant design was used. Three dyads (toddlers with ASD and their primary caregiver) received weekly one-hour home visits from their child's classroom teacher. The intervention was manualized and fidelity was high. The primary outcome measure was taped play interactions of the dyad and this measure was coded by a blinded observer.

**Results:** As a result of the intervention, children used more spontaneous words during play interactions with their caregiver, more joint attention, and more requesting gestures. Effects maintained for 2/3 children and the intervention was favorably perceived by all caregivers.

**Conclusions:** To our knowledge, this is the first pilot investigation of an ASD intervention aimed at improving a core social communication deficit that was taught to toddler caregivers through an Early Intervention teacher. Findings suggest that teachers can successfully instruct caregivers of toddlers with ASD how to improve social communication. This intervention holds promise for inexpensively increasing the focus of community Part C early intervention services on improving core ASD deficits.

**161.163 163** Depression As a Predictor of Decreased Social Engagement for Adolescents with Autism Spectrum Disorder Following the UCLA PEERS® Intervention. C. Costa*, D. Diaz, J. Hopkins, M. Cronin and E. A. Laugeson, *UCLA Semel Institute for Neuroscience and Human Behavior*

Background: Adolescents with Autism Spectrum Disorder (ASD) are known to have deficits in social skills relating to social communication and reciprocity. Impairment in social skills often leads to negative social experiences with peers, including self-reported victimization, which may be associated with greater anxiety and depression (Pouw et al., 2013). In fact, depression is one of the most prevalent comorbidities shown to significantly impair functioning among individuals with ASD (Strang et al., 2011). The Program for the Education and Enrichment of Relational Skills (PEERS®) is an evidence-based, parent-assisted social skills intervention for adolescents with ASD without intellectual disabilities. Previous research indicates that PEERS® is effective in improving social skills and increasing social engagement amongst teenagers on the spectrum (Laugeson et al., 2009; Laugeson et al., 2011). Although PEERS®has a well established evidence-base, there is a lack of research identifying predictors that may impact treatment outcome. In particular, the impact of comorbid depression on social engagement following treatment has yet to be investigated among adolescents with ASD.

Objectives: The present study examines baseline depression as a predictor of social engagement in adolescents with ASD following the completion of a 14-week parent-assisted social skills intervention program.

Methods: Participants included 137 adolescents (113 males and 24 females) with ASD ranging from 11-18 years of age ($M$=13.98, $SD$=1.78) and their parents who presented for social skills treatment through the UCLA PEERS® Clinic. Adolescent and parent participants attended weekly 90-minute group treatment sessions over a 14-week period. In order to assess baseline depression, adolescents completed the Children's Depression Inventory (CDI; Kovacs, 1992) prior to treatment. The CDI includes a total depression score and five subscales including: negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem. In order to assess change in social engagement following treatment, adolescents and parents completed the Quality of Socialization Questionnaire (QSQ; Frankel & Mintz, 2008) pre- and post-intervention. The QSQ measures social engagement with peers through frequency counts of hosted and invited get-togethers in the previous month. Pearson correlations were calculated to examine the relationship between baseline depression on the CDI and change in social engagement on the QSQ from pre- to post-treatment.

Results: Results indicate that participants significantly increased their social engagement following treatment for both hosted get-togethers ($p$<.01) as well as invited get-togethers ($p$<.01) according to adolescent and parent reports on the QSQ. However, higher baseline CDI total scores significantly predict a decrease in the frequency of adolescent-reported invited get-togethers ($p$<.05) following treatment. Results did not reveal a significant relationship between baseline CDI total scores and adolescent-reported hosted get-togethers or parent-reported hosted or invited get-togethers on the QSQ.

Conclusions: These findings suggest that although adolescents with ASD generally improve in their frequency of peer engagement following the PEERS® intervention, those experiencing comorbid depressive symptoms prior to intervention may actually report being invited on fewer get-togethers by their peers following treatment. This finding suggests the need for further intervention to decrease depressive symptoms in those scoring high on the CDI at baseline in order to gain the full benefit of PEERS®.

**161.164 164** Effects of Exergaming on Children with Autism Spectrum Disorders: A Pilot Study. C. L. Hilton*[1], K. Cumpata[2], C. L. Klohr[3] and P. Trapani[4], (1)*University of Texas Medical Branch*, (2)*Children's Medical Center*, (3)*Washington University School of Medicine*, (4)*360 Fitness For Life & Health, LLC*

Background: Although not included in the diagnostic criteria for autism spectrum disorders (ASD), executive dysfunction (Pennington & Ozonoff, 1996), motor impairment (David et al., 2009; Dzuik, et al., 2007; Ghaziuddin and Butler, 1998; Ming et al., 2007) and visual motor integration (Hellinckx, Roeyers & Van Waelvelde, 2013; Sachse et al. 2013) have been frequently observed in individuals diagnosed with ASD. They have immediate limiting effects in childhood and long-term effects into adulthood. Executive function (EF) refers to the higher order control processes that are necessary to guide behavior in a constantly changing environment (Jurado & Rosselli, 2007). Studies of motor skills have generally converged on the notion that 80–90% of children with ASD show some degree of motor impairment. Visual motor integration (VMI) is the

ability to perform complex eye-hand coordination tasks in which perceptual, motor, and cognitive processes interact and has been identified as a predictor of academic performance (Klein, 1978; Kulp, 1999), handwriting quality (Hellinckx, et al., 2013; Kushki, Chau, & Anagnostou, 2011) and driving problems (Keay et al., 2009; Munro et al., 2010). Motor, EF and VMI deficits in children with ASD also contribute to low rates of physical activity participation (Reid, O'Connor, & Lloyd, 2003) and difficulty participating in activities involving constantly changing environments in which fast responses and adjustment need to occur. The Makoto training device was developed for use in performance sports, schools, and medical rehabilitation with goals of improving reaction time, attention, and physical fitness and is classified in the category of *exergames*(games that combine play and exercise; Bogost, 2005).

Objectives: This pilot study investigated the effects of a 30-session Makoto arena training intervention, a light and sound speed-based interactive exergame, on EF, motor skills, and VMI in school age children with ASD.

Methods: 17 children with ASD between 8 and 18 years old participated in this pilot study. A full-scale IQ score of at least 70 and willingness to participate in the Makoto intervention approximately three times per week were required for inclusion in this study. Individuals with lower IQs were excluded to avoid the potential for confusion between impaired intelligence and impaired EF. Participants were evaluated before and after intervention on the Behavior Rating Inventory of Executive Function (BRIEF), the Bruininks-Oseretsky Test of Motor Proficiency-Second Edition (BOT-2), and the Developmental Test of Visual Perception (DTVP-2 and DTVP-A). Average reaction speed was recorded at each Makoto intervention session. Participants completed two minutes of Makoto intervention a minimum of three times per week until thirty intervention sessions were completed, with a total of approximately 1,800 repetitions for each participant.

Results: Participants showed significant improvement in reaction speed, the executive function area of working memory, the motor area of strength and agility, and visual motor integration.

Conclusions: It is important to identify interventions that are both effective and motivating for children with ASD. Findings suggest that the Makoto intervention has the potential to serve as a valuable addition to standard intervention for children with ASD who have EF, motor and VMI impairments. Further study is indicated.

**161.165 165** Efficacy of an Ehealth Parent-Mediated Intervention for Young Children with ASD: Comparison of Two Delivery Approaches. B. Ingersoll*, *Michigan State University*

Background: Parent-mediated intervention for children with ASD has been shown to improve both parent and child functioning. However, access to parent-mediated intervention services is often limited in rural and under-resourced areas. eHealth, the delivery of health information over the internet, has the potential to increase access to parent-mediated intervention in these communities.

Objectives: The goal of this study was to examine the effect of two versions of an eHealth intervention for parents of young children with ASD on parent learning and child social communication skills.

Methods: A randomized control trial was used to examine the effects a self-directed eHealth program used alone (n=15) or in combination with remote coaching (n=15) on parent and child behavior. Children were matched with 3 months of expressive language age on the Mullen and then randomly assigned to the self-directed only (SC-Only) or self-directed plus remote coaching (SD+RC) condition. Parents were given up to 6 months to complete the program. Outcome variables included parent intervention knowledge, parent intervention fidelity during a parent-child interaction in the home, parent-report and observational measures of child social communication skills, and parenting stress. In addition, program usage data was monitored and treatment acceptability was measured at post-treatment.

Results: Preliminary analyses from the first 13 parents indicate high rates of program engagement in both groups with parents completing an average of 92% of program elements. Treatment acceptability rates were similarly high across both groups. There was a main effect of time on parent knowledge and

parent fidelity from pre-post treatment, with parents demonstrating greater knowledge and higher fidelity at post-treatment and pre-treatment. There was a trend for greater gains in both in the SD+RC group. Children in both groups demonstrated significant gains in expressive vocabulary on the M-CDI and social communication skills on the SCC. There was a significant interaction, such that children in the SD+RC group made significantly more gains in standard scores on the socialization domain of the Vineland than the children in the SD-Only group. Parents in both groups showed increased positive feelings towards child, but no change in negative feelings on the FIQ. Exploratory analyses revealed a positive association between treatment acceptability and program elements completed. Program elements completed were associated with change in parent fidelity. Change in parent fidelity was positively associated with changes in positive feelings on FIQ and marginally with Communication Domain scores on Vineland. Parent report of regular use of intervention was associated with improvements in Socialization Domain standard scores on Vineland and words produced on MCDI.

Conclusions: Both approaches show promise for increasing parents' use of evidence-based intervention techniques. Program use and treatment acceptability were high and were associated with gains on parent report measures of child social communication. There was a trend toward greater parent learning and child improvements in the group that received remote coaching. Additional research that can identify parents who are most likely to need remote coaching would assist in the development of a stepped care model that can increase parent access to evidence-based services in underserved communities.

**161.166 166** Efficacy of the Social Adjustment Enhancement Intervention: A Follow-up Study. C. McMahon*[1] and M. Solomon[2], (1)*Indiana University - Bloomington*, (2)*MIND Institute*

**Background:**

Solomon, Goodlin-Jones, and Anders (2004) showed that the Social Adjustment Enhancement Intervention (SAEI) is a promising intervention for increasing social skills in higher-functioning children and adolescents with Autism Spectrum Disorder (ASD). The SAEI curriculum was primarily designed to address deficits in emotion recognition, theory of mind, and executive functions, and thus, Solomon et al. (2004) primarily assessed improvements in these areas.

**Objectives:**

The aim of this study was to more broadly assess the impact of the SAEI on social skills, including social performance (applying social skills appropriately in everyday life), social motivation (interest in social interactions), and social self-efficacy (self-confidence in social skills).

**Methods:**

Twenty-four children and adolescents with ASD, ages 10-16, participated in the current study. Fourteen participants were enrolled in the SAEI. These participants met for 90 minutes/week over 22 weeks and were administered a revised version of the SAEI curriculum (Solomon et al., 2004). Ten participants, matched on age and IQ, were not enrolled in the SAEI and served as a control group. Social skills were assessed before the intervention began, after the intervention ended, and approximately 4.5 months after the intervention ended.

Both child and parent completed the Social Skills Rating System (SSRS; Gresham & Elliott, 1990) as an index of social performance. Additionally, the child completed the Interpersonal Orientation Scale (IOS; Hill, 1987) as an index of social motivation and the Adolescent Social Self Efficacy Scale (ASSES; Connolly, 1989) as an index of social self-efficacy.

**Results:**

There was a significant effect of time on SSRS Social Skills Total for both parent and child report, $F(2, 42) = 3.22$, $p = 0.05$, $\eta^2_p = 0.13$, such that social performance significantly increased from pre-intervention to post-intervention, $F(1, 21) = 4.56$, $p = 0.05$, $\eta^2_p = 0.18$, but did not differ between post-intervention and 4.5 months post-intervention, $F(1, 21) = 0.15$, $p = 0.70$, $\eta^2_p = 0.01$. There was a marginally significant effect of time on ASSES Total, $F(2, 44) = 2.85$, $p = 0.07$, $\eta^2_p = 0.12$, such that social self-efficacy marginally increased from pre-intervention to post-intervention, $F(1, 22) = 3.01$, $p = 0.10$, $\eta^2_p = 0.12$, but did not differ between post-intervention and 4.5 months post-intervention,

$F(1, 22) = 0.03$, $p = 0.87$, $\eta^2_p < 0.01$. Time did not have a significant effect on IOS Total, $F(2, 44) = 2.33$, $p = 0.11$, $\eta^2_p = 0.10$, although the effect may have reached significance with a bigger sample size. Group and the interaction between time and group did not show significant effects in any of the analyses.

**Conclusions:**

This preliminary evidence suggests that both social performance and social self-efficacy increased in participants with ASD from pre-intervention to post-intervention. These increased social skill abilities may be the result of the SAEI, or, as the control group of participants showed a similar improvement, these increased abilities may simply be related to developmental maturation. A randomized controlled trial is an important next step in teasing apart the effects of the intervention versus developmental maturation.

**161.167 167** Generalization of Joint Engagement to the Classroom for Toddlers with ASD Following a Parent-Mediated Intervention. K. Berry*[1], A. Gulsrud[2] and C. Kasari[3], (1)*University of California, Los Angeles*, (2)*UCLA*, (3)*University of California Los Angeles*

**Background:** Children with autism exhibit significant impairment in their ability to engage with their play partner and with toys, including sharing attention between the two (joint engagement). Studies have found children with autism to be primarily unengaged during playtime or solely focused on objects. Several early intervention studies have successfully targeted and reliably measured changes in engagement states, finding significant improvements in engagement type and duration. Previous research has shown that dyads receiving a parent-mediated (JASPER) intervention significantly increased the number of child-initiated play routines and increased the duration of play spent jointly engaged following treatment. However, the extent to which children can generalize these improvements to other play partners and new environments is unknown.

**Objectives:** The goal of this study was to determine if children's improvements in engagement during play following a brief parent-focused early intervention program were generalized cross-contexts. . This is the first early intervention study to observe the child with an adult unfamiliar with the intervention (JASPER) and in a separate environment (the classroom), which allows an exploration of the degree to which *true* generalization of engagement changes occurred.

**Methods:** Eighty-six parent-child dyads were recruited from an intensive early intervention program that provides 30 hours per week of treatment in a classroom setting. Children were between 18 and 33 months old ($M$=31.5) with an autism diagnosis and mean IQ of 68. Parent-child dyads were randomized to receive either a parent-mediated intervention (JASPER) or a parent-education condition (focused on reducing stress and informing parents on development, behavior, etc.) (Brereton & Tongue, 2006) in addition to their 30 hour per week classroom treatment. All participants met one-on-one with a trained interventionist weekly for 10 weeks**.** Live classroom observations were collected pre and post treatment while the child played with their teacher who was not trained in the intervention techniques and blind to child condition.

**Results:** Results indicate that children randomized to the parent-mediated (JASPER) intervention showed a significant interaction effect of time and treatment for joint engagement ($F(1, 79) = 5.46$, $p$=0.02). There was also significant effect of time on decreasing disengagement ($F(1,79) = 14.78$; $p$= 0.0002), yet there was no significant interaction effect ($F(1,79) = 1$; $p$= 0.3195).

**Conclusions:** This study is the first to directly observe child behaviors both within a novel environment and with a novel (untrained) play partner as generalization from a parent-mediated intervention. Other studies have gathered reports from teachers on child engagement with less robust effects of intervention (e.g, Green et al, 2010). In addition, participants were recruited from the same comprehensive and intensive early intervention program, which provides a unique ability to observe children in their classroom and allows valid examination of child behaviors as related to their treatment assignment. These data suggest that while a parent-mediated intervention can directly improve child outcomes (Kasari et al., 2006, 2008, 2010, 2012) it may also produce effects robust enough to transcend the context in which they were taught and generalize to other

play interactions, thus changing social interactions with new play partners.

**161.168 168** Integrating Behavioral Strategies for Children with Autism. A. B. Jobin*[1], L. Schreibman[2] and A. C. Stahmer[2], (1)*Rady Children's Hospital San Diego*, (2)*University of California, San Diego*

Background: Treatment studies indicate that substantial gains may be achieved by some children with autism spectrum disorders (ASD) when behavioral treatment is provided at an early age. However, heterogeneity of treatment response is common to all evidence-based approaches. Currently, no treatment completely ameliorates the symptoms of ASD and no specific treatment has emerged as the established standard of care. Investigators have hypothesized that customizing treatments based on individual child and family needs should increase the overall number of children that benefit from intervention. Improved understanding of how to match specific treatments (e.g., Discrete Trial Training, Pivotal Response Training) to children exhibiting different behavioral characteristics may enhance our ability to tailor interventions to individual children, thereby improving treatment effectiveness.

Objectives: (1) To evaluate the relative effectiveness of Discrete Trial Training (DTT) and Pivotal Response Training (PRT) for teaching children with autism under the age of 3 receptive and expressive language, play, and imitation skills, and (2) to identify variables influencing whether specific children are more likely to benefit from DTT or PRT in the tested domains.

Methods: A single-subject adapted alternating treatments design was used, whereby children received both DTT and PRT for 12 weeks. Language, play, and imitation targets were matched on developmental appropriateness and difficulty and then randomly assigned to treatment conditions. Potential predictor variables were collected at pre-treatment. Fidelity measures were collected on 33% of all procedures. Data are reported on rate of learning, spontaneous skill use, as well as skill acquisition and generalization during weekly probes, and maintenance of gains at 3-month follow-up.

Results: All participants learned target skills in both treatments and demonstrated some generalization, maintenance, and spontaneous use of skills acquired during DTT and PRT. However, each child benefited to differing degrees from intervention. PRT was more effective for some children, domains, and dimensions of behavior, whereas DTT was more effective for others. The results also suggested that a combination of PRT and DTT may be optimal in some cases. Pre-treatment adult avoidance and language skills may aid in prospective treatment planning efforts. Additionally, early rates of learning may be predictive of longer-term treatment response.

Conclusions: The results confirm the importance of treatment individualization and begin to suggest specific methods for tailoring treatment programs to individual child needs. The strengths and weakness of DTT and PRT may vary depending on child variables, as well as curriculum area focus.

**161.169 169** Moderators of Short-Term Effects and Maintenance from Social Cognitive Group Therapies: Results from a Randomized, Comparative Trial of Seaver-Nett. L. Soorya*[1], A. T. Wang[2], P. M. Weinger[3], J. D. Buxbaum[3], D. B. Halpern[3] and M. Gorenstein[3], (1)*Rush University*, (2)*Seaver Autism Center*, (3)*Icahn School of Medicine at Mount Sinai*

Background: Several recent reviews indicate social skills groups are evidence-based interventions for verbal school-aged children with ASD. To date, the majority of studies have compared outcomes in treatment groups to no-treatment or wait list control immediately following treatment.

Objectives: The purpose of this analysis was to evaluate 3-month outcomes and moderators of treatment effects from two models of social skills group interventions: 1) social cognitive behavioral therapy (Seaver Nonverbal synchrony, Emotion recognition, and Theory of mind Training); and 2) child-directed play. Outcomes included immediate (12-week) and maintenance (3-month no treatment follow-up). Both neural (e.g., fMRI) and behavioral outcomes were collected with behavioral data highlighted in this abstract.

Methods: Participants (n=69), ages 8-11 were randomized into Seaver-NETT or comparison conditions. Both treatments involved 12, 90-minutes sessions, with concurrent parent and child intervention groups. Outcomes were conducted at baseline, endpoint, and at a 3-month follow-up visit to assess maintenance. Outcomes included blinded, direct assessments of

social cognition (e.g. DANVA2, RMET, Strange Stories) and caregiver reports of social behavior (e.g. Griffith Empathy Scale, CCC social and nonverbal subdomains), as well as neural processing of emotions in faces and voices. Linear mixed models, with age and IQ entered as moderators, were used to evaluate treatment effects on derived composite scores of social behavior and social cognition.

Results: Results from analysis of *social behavior* composites suggest age and IQ were significant moderators of group X time effects. Older children in the CBT intervention showed improved ratings at endpoint ($p=.032$) relative to the comparison intervention. The interaction effect was no longer significant at 3-month follow-up although scores did not revert back to baseline levels ($p=.14$). No effect of time, age, or IQ was found for the comparison condition. Results from analysis of *social cognition* composites suggest a main effect of IQ across groups ($p<.00$) but not on the interaction. A trend towards improvement on social cognition composites was found for IQ for children enrolled in the social cognitive intervention ($p= .10$), with follow-up analyses indicating significant improvements at endpoint on low-intensity (difficult to identify) child faces on the DANVA2 ($p<.01$).

Conclusions: This study supports a growing body of literature suggesting positive short-term outcomes from CBT-based social groups, primarily in the domain of social competency rather than social cognition (Reichow, et al., 2012). Descriptive data suggest gains in ratings of social behavior relative to baseline at 3-month follow-up for both groups, although changes were not statistically significant. Age and IQ were significant moderators of treatment effects for social behavior, and IQ only on main effects of social cognition. Intermediate effects of Seaver-NETT were observed on neural measures of processing irony and eye gaze (Wang et al., 2013). In contrast, trends on behavioral tasks of social cognition were not significant, indicating a need for augmentative treatment models for social cognitive deficits in ASD.

**161.170 170** Preliminary Data on Individualized Social Skill Outcome Measures Associated with the START Group Social Skills Intervention for Adolescents with ASD. A. R. Miller*, T. L. Clarke, M. K. Cornish, K. P. Dresser, M. R. Fredricks, K. D. Russo, V. L. Wu, J. L. Bradshaw, A. Navab and T. W. Vernon, *University of California Santa Barbara*

Background: "High-functioning" adolescents with ASD are especially susceptible to limited access to crucial intervention services. These individuals often continue to have limited social success and difficulty with basic conversation skills, all while entering a developmental phase associated with increasingly complex social situations. Intervention at this stage is clearly essential to promote healthy outcomes. Social skills interventions have increased in popularity in recent years, with growing empirical evidence for their effectiveness (National Autism Center, 2009). Many of these interventions have been held in group formats to increase treatment availability while simultaneously providing opportunities for built-in peer practice (Barry et al., 2003). There is limited research, however, on the ideal format of social skill interventions to maximize therapeutic benefit.

Objectives: Our current study evaluates the effectiveness a novel, multi-component group social skills intervention (START) for adolescents with ASD. The START program blends several established and novel treatment components, including motivational procedures, self-management, tailored individual target goals, an experiential format, and inclusion of typically developing peer facilitators.

Methods: A repeated measures design was used to closely monitor participants' social growth trajectories across two pre-intervention time points and serial reassessment after every five sessions of the START program. Participants were adolescents with a previous diagnosis of an ASD, conversational language use, and a verbal IQ above 70. The START program occurred weekly, and consisted of the following components: an individual check-in session, group socialization, group activity, group discussion of a social skill topic, role play, practice, an individual check-out session with parent involvement, and homework assignments to be completed between group sessions. In addition to the group curriculum, individual social skills were targeted for each participant (e.g. on-topic question-asking, on-topic comments, initiations, introduction of novel topics, elimination of negative statements, and equitable speaking time between conversation partners). Multiple forms of measurement were

used to obtain a comprehensive picture of participants' social competence, including direct observations of naturalistic conversations, parent report (SRS, SSIS), and adolescent self-report (SSIS). The direct observations also serve as measures of generalization, as this data was gathered outside of the START setting with unfamiliar peers.

Results: The results of the study indicate that all socialization measures significantly improved following ongoing implementation of the START program. Data from several parent-report and adolescent self-report measures indicate significant social skill improvement. This poster highlights the improvement in individual target skills exhibited through direct observations of naturalistic conversations between participants and unfamiliar peers. Graphs of individual target skills show stability before intervention and improvement during participation in the START program, indicating generalization of social skill improvements. Medium to large effect sizes were observed across the majority of dependent measures.

Conclusions: The preliminary START program target skill data provides strong evidence for its use as an effective group social skills intervention for adolescents with ASD. The incorporation of several unique components—peer facilitators, an experiential format, and the use of self-management to target individual skills—appear to directly drive improvements to all social measures, including generalized changes to directly observed social skill application in naturalistic settings.

**161.171 171** Preparing for University Life: A Program Evaluation. A. J. Hillier*[1], J. B. Kopec[2] and S. M. Donnelly[1], (1)*University of Massachusetts Lowell*, (2)*Northeastern University*

Background: Adolescents and young adults on the autism spectrum are attending university in rapidly increasing numbers. While academically many excel, social and executive functioning challenges, as well as severe anxiety can impede their success. Preparing high school students in advance for the realities of university life, the academic expectations, the social challenges, and the many ways in which university differs from high school is crucial preparation for this transition.

Objectives: This study aimed to evaluate the efficacy of a college preparation mentoring program for high school students with autism spectrum disorders.

Methods: Forty-seven adolescents (39 Males, 8 females) between the ages of 16 and 22 years (average age: 18 years) participated in a 6-week college preparation mentoring program. Nine cohorts completed the program over a four year period. Program sessions were an hour once a week and participants met on a university campus with a current university student who served as a mentor. The program curriculum consisted of a range of topics including time management, campus support services, choosing a major, class schedules, and socializing on campus. Activities included a campus tour, visiting a dorm, and attending a lecture. Participants completed a questionnaire before and after the program consisting of both quantitative (Likert scale) and qualitative items.

Results: Responses on the questionnaire indicated significant positive outcomes in a number of areas following participation in the program. On the quantitative Likert scale questions, participants reported a significantly greater understanding of what to expect at university, were looking forward to attending university to a significantly greater extent, indicated significantly improved knowledge of how things work at university, how to access support services, and what a lecture will be like. Concern about their performance at university was not alleviated however. There was not a significant change in responses to how worried they felt about going to university, and they were slightly more worried that they might not do well academically (perhaps reflecting a more realistic perspective of university level expectations). Positive outcomes were supported in the qualitative responses to open ended questions. In categorizing responses, participants mentioned social concerns less frequently at the end of the program, were less concerned about the dorms, had a better understanding of available support services, and felt better prepared for university.

Conclusions: Our university preparation program was successful in helping high school students with ASD improve their understanding, knowledge, and enthusiasm regarding transitioning to university. The program model

has a number of key advantages including the cost effectiveness and the inclusion of peers as mentors for the program participants. Qualitative responses on the evaluation questionnaire clearly articulated the effectiveness of having a "real student" explain the realities of university life. We hope this model will be replicated at other universities and ultimately improve the success and retention of young adults with ASD in academia.

**161.173 173** Social and Emotional Functioning in Autism and Anxiety: Participation in a Social Competence Intervention in a Private Clinical Setting. S. I. Habayeb*[1], B. Rich[1] and M. Alvord[2], (1)*The Catholic University of America*, (2)*Alvord, Baker, & Associates*

Background: In the development of evidence-based intervention programs, efforts must be made to lessen the gap between clinical and research practice (Kazdin, 2008). Child research samples from controlled laboratory settings are not necessarily representative of populations typically receiving services in community settings. Indeed, research finds that youth treated in clinical service settings, as compared to youth treated in academic research settings, have greater diagnostic heterogeneity and greater severity of symptoms (Ehrenreich-May et al., 2011). As a precursor to understanding the impact of psychotherapeutic interventions, it is essential to first understand the populations of children receiving such services in clinical settings. This need to better define youth receiving therapy is particularly acute in children with high functioning autism spectrum disorders (HFASD), given that they are frequently treated in community settings and present with prominent comorbidity, in particular anxiety disorders (AD; Leyfer et al., 2006).

Objectives: To understand manifestations of anxiety in children with HFASD (and in comparison to children with AD) in regard to social and emotional functioning in order to better predict outcomes of targeted interventions in clinical service settings.

Methods: 14 children with HFASD (mean age, 10.96 years) and 23 children with AD (mean age, 10.31 years) with significant social impairments were treated in a large private practice with the Resilience Builder Program®, a manualized group therapy that targets social competence and resilience-based skills. Pre-treatment parent- and child-report included the Behavior Assessment System for Children, 2nd Edition (BASC-2; Reynolds and Kamphaus 2006), which measured social, emotional and behavioral functioning, and The Social Skills Improvement System-Rating Scales (SSIS-RS; Gresham and Elliot, 2008), which measured social functioning.

Results: HFASD and AD youth had comparable levels of child- and parent-reported anxiety symptomatology ($t=-0.78$, $p=0.44$ and $t=-1.45$, $p=0.16$ respectively), however, HFASD youth reported significantly greater social deficits than AD youth ($t=2.12$, $p=0.04$). Child-reported anxiety symptoms were strongly related to child-reported social stress in both groups (HFASD: $r = 0.66$, $p= 0.01$; AD: $r = 0.57$, $p < 0.01$). Finally, while child-reported social stress was associated with parent-reported emotion dysregulation in the HFASD group ($r = -0.54$, $p= 0.04$), there was no such relationship in the AD group ($r = -0.24$, $p = 0.27$).

Conclusions: In this population of children presenting in a private practice for a resilience-based manualized group therapy, similar behavior profiles emerged between children with HFASD and AD in terms of anxiety and social stress. However, whereas greater social stress was associated with emotional regulation deficits in HFASD youth, AD youth did not display such a relationship. These results suggest that emotion dysregulation may play a prominent role in the social distress seen in HFASD youth and thus is a worthy target of intervention. In order to lessen the gap between clinical and research practice, characterization of populations of children obtaining services in clinical settings is important in order to best tailor interventions to underlying maladaptive motivations and behaviors.

**161.174 174** The Effects of a Parent-Mediated Early Toddler Intervention on Improving Language Trajectories and Joint Attention. J. L. Bradshaw*, H. E. Reshes, A. Navab, A. R. Miller, T. W. Vernon and L. K. Koegel, *University of California Santa Barbara*

Background: Sensitivity and specificity for determining early risk for ASD has improved in recent years with the age of stable diagnosis rapidly approaching 18-24 months. Early diagnosis necessitates empirically based early intervention programs for infants and toddlers under two years of age. Effectiveness of early intervention for infants and toddlers is dependent

on both improving child outcomes and documenting feasibility and parent acceptability. Thorough investigation of intervention models for toddlers with ASD, including analysis of language trajectories, improvements in joint attention, feasibility, and acceptability, is needed to further our knowledge of the implications of early treatment for toddlers.

Objectives: This study aims to investigate the effects of a brief, naturalistic, parent-mediated intervention using the motivational strategies of Pivotal Response Treatment by: 1) examining changes in toddler language trajectories, including the frequency and quality of functional communication, 2) exploring collateral gains associated with emergence of language, including joint attention, and 3) analyzing the feasibility and parent acceptability of the intervention.

Methods: Participants in this study were toddlers between 15-20 months who exhibited high risk for ASD, including ADOS-T classification of ASD, expert clinical judgment of ASD, and no functional language. Treatment was implemented in the home one hour per week for approximately 12 weeks. Effectiveness of the intervention was evaluated using a multiple baseline design across three participants. Weekly measures of language use were recorded including frequency, form (initiation or response), and function (request or comment, i.e. joint attention). Feasibility and acceptability were analyzed with parent fidelity of implementation and social validation questionnaires, completed anonymously by the parents. Gains in standardized measures (ADOS, Mullen, and Vineland) were also analyzed.

Results: All toddlers were minimally verbal prior to the start of intervention and demonstrated low levels of functional communication in naturalistic interactions, resulting in a mean frequency of communication (MFC) of 2.2 (SD=2.7) across baseline. Upon implementation of the intervention toddlers demonstrated dramatic gains in verbal communication (MFC=41.7, SD=16.7), including increases in frequency of both initiations (M=20, SD=9) and responses (M=21.6, SD=9.1). Analysis of language trajectories indicated that participants initially communicated in order to request (the primary target of the intervention) and gradually began to initiate joint attention, in the form of commenting. Results of the fidelity of implementation measures and parent satisfaction questionnaires indicated satisfactory feasibility and acceptability across all participants. Finally, standardized assessments support observed findings as all toddlers improved in measures of language, socialization, and autism severity.

Conclusions: These results suggest that a language-based PRT intervention model for 15-20-month-old toddlers at-risk for ASD has significant implications for improving developmental trajectories. Following intervention, toddlers exhibited rapid increases in the quantity and quality of functional verbal communication. The consequential development of verbal initiations, including initiation of joint attention, suggests that the intervention was effective in improving overall social motivation. Furthermore, all toddlers made notable gains in standardized measures of language, socialization, and autism severity. This treatment proved both feasible and acceptable as all parents met fidelity of implementation, found the intervention easy to implement, and reported to enjoy the intervention.

**161.175 175** The Pegasus Psychoeducational Programme for Young People Diagnosed with Autism Spectrum Disorder Enhances ASD Self-Awareness. K. Gordon*[1], L. Roughan[2], O. Baykaner[2], V. Livermore-Hardy[3], D. H. Skuse[1], M. Murin[2] and W. Mandy[1], (1)*UCL Institute of Child Health*, (2)*Great Ormond Street Hospital*, (3)*Great Ormond Street Hospital, London*

Background: There are several potential benefits of receiving an ASD diagnosis including access to funding and appropriate treatments. Increasing self-understanding and positive self-perception are additional important benefits for adults which have not been found to extend to children. One way to counter the phenomenon of young people feeling disengaged from or stigmatised by their ASD diagnosis is to offer them psychoeducation. Whilst psychoeducation is recognised as a *sine qua non* of good post-diagnostic care in ASD, there is currently no evidence-based practice in this area.

Objectives: We designed a manualised psychoeducational programme to teach young people with ASD about their diagnosis (level one psychoeducation) and to help them use this information to develop insight into their own unique collection of strengths and difficulties (level two psychoeducation). This programme is called PEGASUS - 'PsychoEducational Groups for Autism Spectrum Understanding and Support. It is

administered in six weekly group sessions, with parallel parent groups. PEGASUS has a strong focus on strengths, conveying the message that having ASD involves being different, but not inferior, to people without ASD.

Methods: 48 children (9-14 years) with a diagnosis of ASD and their parents were recruited into a randomised control trial (RCT). Half were randomised to attend the PEGASUS groups and half to the control group, in which they were offered "treatment as usual" (TAU). Five PEGASUS groups each including 4-6 children were run. Primary outcomes were evaluated using the 'Measure of ASD Understanding and Self-Awareness' (MAUSA). Secondary outcome measures included the Rosenberg Self-Esteem Scale. Measures were collected blind, pre and post intervention.

Results: *PEGASUS increased knowledge about ASD:* Bootstrap multiple regression, controlling for ASD knowledge at baseline, showed a significant effect of group on ASD knowledge at follow up, β=.29, p<.001, 95% CIs [.13, .44]. *PEGASUS increased ASD self-awareness:* There was a significant and substantial effect of group on the number of ASD strengths and difficulties listed by participants at follow up, controlling for this measure at baseline, β=.42, p=.001, 95% CIs [.17, .67]. This reflected a higher number of both ASD strengths (β=.41, p=.002, 95% CIs [.15, .67]) and ASD difficulties (β=.34, p=.001, 95% CIs [.08, .60]) listed by PEGASUS participants at follow up. *PEGASUS did not change self-esteem or co-occurring symptoms of psychopathology:* Controlling for baseline measures there was no effect of PEGASUS on self-esteem by self (β=.10, p=.404, 95% CIs [-.14, .35]) or parent (β=.12, p=.324, 95% CIs [-.12, .36]) report.

Conclusions: After PEGASUS, participants were able to name more autism-related strengths as well as autism-related difficulties compared to controls. ASD knowledge was also significantly higher in the PEGASUS group compared to the control group. Further, participants in PEGASUS did not show any reduction in self-esteem. This is an important finding, indicating that increasing insight about ASD facilitates the potential for self-efficacy and does not impact negatively on self-concept. This study is the first RCT to show the efficacy and benefits of using post-diagnostic psycho-education groups.

**161.176 176** Educator and Student Response to a Social-Communication Intervention Translated for Public Preschool Classrooms. K. P. Wilson*, E. Stripling and R. Landa, *Kennedy Krieger Institute*

**Background**: There is a pressing need for efforts to translate efficacious lab-based interventions into accessible interventions for public school settings serving young students with ASD. Bringing such effective interventions into early childhood classrooms could lead not only to improvement in child outcomes, but also to reductions in long-term education costs for the growing body of students with ASD. The 'Early Achievements' (EA) intervention model was honed in the lab setting to improve interpersonal synchrony and communication functioning in toddlers with ASD. This model was proven effective through an RCT (Landa et al., 2011) and treatment gains were maintained for 6 months following the intervention period. The EA model is now being translated for use in public preschools through funding from the Institute for Educational Science.

**Objectives**:

(1) To describe the training and coaching procedures, as developed from a lab/clinic into community based model.

(2) To examine changes over time in trained educators' fidelity of implementation of the EA intervention in response to training and coaching.

(3) To examine preliminary results reflecting student change.

**Methods:** Mixed methods were used to address the aims. Focus groups and structured participant feedback informed development of training and coaching procedures, as well as adaptations of the lab-based intervention model for use in public school classrooms. Quantitative longitudinal fidelity of implementation data were collected for teachers and instructional assistants from two participating classrooms over eight months. Videotaped data were coded by research staff blind to classroom characteristics and time point, with an average of 17 datapoints per educator. Data for 18 participating students with ASD were collected through the Mullen Scales of Early Learning and an experimental joint attention task at the beginning (prior to educator training) and end of the school year.

**Results:** Qualitative focus group results indicate multiple practical barriers to implementation of the lab-based EA intervention model. These barriers (e.g., limited resources, varying levels of pre-service training in ASD) will be outlined along with adaptations to the EA intervention that address each barrier and the resulting training and coaching procedures. Data reflecting fidelity of implementation of key aspects of the adapted EA model across the school year (before, during, and following training/coaching) indicate mean gains of 70% for teachers and 65% for instructional assistants, with all educators meeting fidelity criteria for the EA strategies. Pre-post student gains on the Mullen Scales of Early Learning were significant across scales (Visual Reception, *p=.0021*; Fine Motor, *p=.0028*; Receptive Language, *p=.016*; Expressive Language*, p=.0185*) and significant improvements in response to joint attention points were seen (p=.0222) during an experimental task.

**Conclusions:** Combined preliminary results indicate feasibility of the adapted EA intervention model, based on four educators' uptake of the strategies in their classrooms. In addition, student data indicate the potential impact of the preschool educators' use of the EA strategies during classroom instruction. Implications will be discussed in terms of next steps within this intervention development study, as well as for a future, larger-scale efficacy trial.

**161.177 177** Video-Based Instruction to Improve Job-Related Problem-Solving Skills of Students with Autism. G. Yakubova*, *Duquesne University*

Background:

Consistent poor employment outcomes among individuals with autism persist and limited research exists on how best to support high school students with autism in preparing them for employment (Shattuck et al., 2012). Additionally, instructions incorporating video technology are promising to improve various skills of students with autism (Bellini & Akullian, 2007). However, limited research exists instructing students with autism to engage in problem solving. This presentation will describe the benefits of using video-based instruction for students with autism and teaching how to solve problems encountered during job-related tasks.

Objectives:

The purpose of this study was to determine the effectiveness of a problem solving intervention on improving problem solving performance of students with autism during vocational tasks. The following research questions were addressed: To what extent do students with autism use problem-solving steps when solving problems during job-related tasks between the baseline and intervention phase? To what extent do students with autism generalize the use of problem-solving steps to solving problems in an untrained setting? To what extent do students with autism maintain problem-solving skills six weeks following conclusion of the intervention phase?

Methods:

A single-subject methodology, multiple-probe across students design (Horner & Baer, 1978), was used to determine the effectiveness of using video-based instruction to teach problem solving to four high school students with autism when working on various job-related tasks. Data were analyzed using visual analysis to determine whether a causal relationship existed between the problem solving intervention and students' problem solving performance. Additionally, the improvement rate difference was used to calculate an effect size. To further supplement visual analysis, All Pair-wise Comparisons for Unequal Group Sample Sizes (Dunn, 1964) was used to provide statistical evaluation of the extent to which the changes occurred across phases.

Results:

Results demonstrated the effectiveness of the intervention on improving all students' problem solving performance across all problem categories. Effect size measures revealed a strong effect for each student between baseline and intervention across all problem types. Statistical analysis resulted in significant difference between baseline and intervention for each student per problem type. Generalization of problem solving performance to a second untrained setting was evident for each student and resulted in a strong effect size measure. Additionally, three of four students maintained problem solving performance at a six-week follow-up. Validity for this intervention was provided through comments from teachers and students in both schools.

Overall, evidence supported that students with autism can independently engage in problem solving following the intervention.

Conclusions: This study expands previous research on improving employment-related skills of transition-age youth with autism and contributes to limited research on improving problem solving skills of students with autism. Overall, results suggest that embedding opportunities for problem solving within a functional curriculum improves students' independent performance on vocational tasks. To improve poor post-school outcomes of individuals with autism, problem solving should be included in students' individualized transition plans and taught within three major transition domains: post-secondary education/training, employment, and daily living.

**161.178 178** Effects of Dyadic Peer-Relationship-Oriented Intervention for Chidren with High-Functioning ASD. H. Fujino*, *Tokyo Gakugei University*

Background: Friendship has important influences on children's social development, and having a friend serves as a source of emotional support and protection from loneliness and social rejection (Bauminger et al., 2008). We hypothesize that sharing positive experiences through activities performed with a particular peer for a certain period of time promotes social development and mental health in children with high-functioning autism spectrum disorder (HFASD).

Objectives: We developed an intervention program to facilitate peer relationships in school-aged children with HFASD. This program was characterized by a "buddy system" comprising pairs of children with ASD. We report the outcome of this intervention.

Methods: Participants included 42 children (34 male, 8 female) with ASD from the second to the fourth grade (ages 8–10) and their parents. The average full scale IQ was 102 on the Wechsler Intelligence Scale for Children-III. All the children received treatment at Tokyo Children's Rehabilitation Hospital. Twenty-two children (eleven fixed pairs) received the intervention, which consisted of regular treatment in addition to our program. The other twenty children, the waiting-list control group, received regular treatment only. The intervention, consisting of 16 sessions conducted once every two weeks, included training in conversation and emotional regulation skills, play activities with one's buddy, and game activities in which all the participants gathered together and competed with other pairs. Supporters facilitated positive interaction among the children. Parents of all the children responded to the Child Behavior Checklist (CBCL/4-18) and the Strengths and Difficulties Questionnaire (SDQ) before and after the intervention period. The scores for "peer problems" (SDQ), "prosocial behavior" (SDQ), and "social problems" (CBCL) were measures for social development, and those for "emotional symptoms" (SDQ), "withdrawn" (CBCL), and "anxious/depressed" (CBCL) were measures for mental health.

Results: A two-way mixed ANOVA (2 (group: intervention versus control) × 2 (time: pre- versus post-intervention)) was conducted. The main effects of group were found in "peer problems," "prosocial behavior," "social problems," "withdrawn," and "anxious/depressed." There were significant amounts of change in the scores in the post-assessment. Moreover, the interaction between age and the presence of ASD was significant only in "prosocial behavior" ($F(1, 40) = 4.14$, $p < .05$). The simple main effect of group ($F(1, 40) = 8.70$, $p < .01$) was significant. There was a significant amount of change in the scores in prosocial behavior in the intervention group compared to the control group.

Conclusions: A significant improvement was observed for "prosocial behavior" in the intervention group compared to the control group. This SDQ subscale evaluates caring for others, sharing, support, and kindness. "Peer problems," "emotional symptoms," and "withdrawn" also improved in the intervention group, but the results for these were not more significant than those of the control group. These results suggest that the experience of engaging in activities with a particular peer for a certain period of time may facilitate empathy and supportive behavior toward another person in children with HFASD.

**161.179 179** Effects of Social Stories for Individuals with ASD: A Quantitative Review. C. Qi*[1], E. E. Barton[2] and Y. L. Lin[1], (1)*University of New Mexico*, (2)*Vanderbilt University*

**Background:** Delayed social communication skills and restricted and repetitive behavior are the recognized characteristics of ASDs (American Psychiatric Association, 2013). Although there is a burgeoning set of evidence-based practices (EBPs)

related to positive outcomes for children with ASD (National Autism Center, 2009), there also exists a plethora of alternative, fad, or complementary interventions related to ASD. Due to the fast increase in the prevalence of ASDs, there is a growing demand for EBPs. Although several reviews of social story-based interventions have been published, the findings across reviews were not consistent.

**Objectives:** The primary goal of this study was to provide a quantitative synthesis of the effectiveness of social stories intervention for individuals with ASD. Specifically, this review will: (a) evaluate whether each study met the What Works Clearinghouse (WWC) design standards, (b) determine the strength of the evidence using a set of visual-analysis-based evidence criteria, (c) calculate multiple nonoverlapping indices scores, and (d) establish whether the social stories intervention might be an EBP.

**Methods:** Studies were identified using Academic Search Complete, Education Research Complete, PsychINFO, and the Education Research Information Center (ERIC). Inclusion criteria were: (a) the author(s) included at least one participant with ASDs; (b) studies were published in an English language, peer-reviewed journal prior to July 2013; (c) the authors used a single-case research design (SCRD); (d) the study included a graphic display of outcomes; and (e) social stories were the sole intervention. Twenty-two studies met the inclusion criteria for review.

**Results:** First we evaluated the quality of methodology of research. Only 4 studies met the WWC design standards and 18 met design standards with reservations. Second, the WWC evidence criteria (based on visual analysis) were used to determine whether there was a functional relation between social stories and the outcome variables. Only one study provided strong evidence, 6 provided moderate evidence, and 15 provided no evidence. Third, four nonoverlapping indices including percentage of nonoverlapping data (PND), percentage of data exceeding the median (PEM), percentage of data exceeding the median trend line (PEM-T) and pairwise data overlap squared ($PDO^2$) were calculated. The overall median PND of 70%, the mean PEM of 78%, PEM-T of 70%, and the mean $PDO^2$ of 82% for the intervention phase placed social stories in the effective range based on the criteria set by Scruggs and Mastropieri (1998). Finally, the WWC guidelines (5-3-20) were used to determine whether social stories were evidence based (Kratochwill et al., 2013): (a) a minimum of five SCRD studies that met standards or met standards with reservations, (b) studies conducted by at least three independent research groups, and (c) at least 20 individual demonstrations of an effect (Kratochwill et al., 2013). Studies included in this review met all three criteria, thus, social stories intervention were considered evidence based.

**Conclusions:** It is important to continue to explore SCRD synthesis methods in conjunction with visual analysis and clinical judgment to identify evidence-based practices for individuals with ASD.

**161.180 180** Empathy As a Predictor of Treatment Outcome in Young Adults with ASD Following the UCLA PEERS® Intervention.

E. M. Shipley*[1], Y. Bolourian[2], S. Bates[3] and E. A. Laugeson[2], (1)*The Help Group - UCLA Autism Research Alliance*, (2)*UCLA Semel Institute for Neuroscience and Human Behavior*, (3)*Pepperdine University*

Background:

Young adults with Autism Spectrum Disorder (ASD) are known to have social deficits which often impede their ability to develop meaningful relationships. However, increased empathic skills may be associated with better overall social functioning, possibly enhancing relationships with others. Although few evidence-based social skills interventions exist for young adults with ASD, one treatment has been shown to significantly increase social responsiveness, overall social skills, peer engagement, and empathy. The *Program for the Education and Enrichment of Relational Skills (PEERS®) for Young Adults* is an evidence-based, caregiver-assisted social skills treatment targeting relationship skills in young adults with ASD without intellectual disabilities. While this program has been empirically-supported for youth with ASD, the complex relationship between empathy and treatment outcome has yet to be explored.

Objectives:

The present study seeks to examine how baseline empathy in young adults with ASD impacts treatment outcome in a caregiver-assisted social

skills intervention targeting the development and maintenance of relationships.

Methods:

Thirty-two young adults with ASD, ranging from 18-28 years of age (*M*=20.6; *SD*=2.1), and their caregivers participated in concurrent weekly 90-minute group treatment sessions over a 16-week period. Skills were taught through didactic instruction using concrete rules and steps of social etiquette in conjunction with role-playing exercises, in-session behavioral rehearsal activities, and caregiver-assisted weekly socialization homework assignments. In order to assess baseline empathy, caregivers completed the Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004), which assesses empathy levels among adults with ASD, prior to treatment. Treatment outcome was assessed using a battery of caregiver-reported measures including the Social Responsiveness Scale (SRS; Constantino, 2012), the Social Skills Rating System (SSRS; Gresham & Elliott, 2008), and the Quality of Socialization Questionnaire (QSQ; Frankel & Mintz, 2008) pre- and post-intervention. Pearson product-moment correlation coefficients were computed to assess the relationship between baseline empathy and treatment outcome following intervention.

Results:

Results indicate that baseline caregiver-reported empathy, as measured by the EQ, significantly predicts treatment outcome on the SRS in the areas of social awareness ($p<.05$). and social cognition ($p<.05$), with a trend for overall social responsiveness ($p<.08$). Baseline empathy on the EQ also predicts treatment outcome of the SSRS in the areas of cooperation ($p<.05$), responsibility ($p<.05$), and externalizing ($p<.05$), in addition to increased peer engagement through invited get-togethers from peers on the QSQ ($p<.01$).

Conclusions:

These findings suggest that better empathic abilities prior to treatment may result in stronger treatment outcomes for young adults with ASD following the PEERS® for Young Adults intervention. In particular, greater improvement may be observed in the areas of social responsiveness, overall social skills, and peer engagement. These findings are useful in distinguishing those who may be more likely to receive greater benefits from targeted social skills treatment.

**161.181 181** Examining the Effects of a Comprehensive Reading Intervention for Adolescents with ASD. C. K. Reutebuch* and F. El Zein, *The University of Texas at Austin*

Background:

The Center on Secondary Education for Students with ASD (CSESA) is conducting a line of research to develop and evaluate a comprehensive school-based intervention program. One of the intervention components being developed and evaluated targets improving academic achievement by increasing comprehension through the use of peer-mediated strategies. Reading comprehension is important to academic success and quality of life (Carnahan & Williamson, 2010), however previous reading intervention studies with students with ASD have focused on decoding and sight word recognition (Chiang & Lin, 2007; Whalon & Hanline, 2008). Many students with ASD have unique profiles of reading performance exhibiting strengths in basic reading skills coupled with difficulties in reading comprehension (Asberg, Kopp, Berg-Kelly, & Gillberg, 2010; Chiang & Lin, 2007; Nation, Clarke, Wright, & Williams, 2006). Despite the deficits n reading comprehension for many in this population, previous interventions have targeted challenging behavior and communication skills while neglecting academic achievement.

Objectives:

We conducted a pilot study with three participants to investigate the reading, behavioral, and social outcomes of implementing an evidence-based reading comprehension intervention adapted for high school students with ASD.

Methods:

A delayed multiple baseline design was employed across three students across all phases (baseline, intervention, and maintenance). Data was collected on the following dependent variables: (1) task completion, (2) accuracy of responding, (3) social interactions, and (4) challenging behaviors. Students with ASD worked with a peer-pair to learn and apply the comprehension reading intervention strategies with text provided by the

researchers. Researchers implemented 30-minute sessions twice a week. The targeted student also received a strategies tutorial session and review once a week. Fidelity observations and debrief meetings were conducted daily. Data for the dependent measures was analyzed in terms of visual analysis and percentage of non-overlapping data. PND scores were interpreted based on the following set of criteria: (a) more than 90% of PND = very effective treatment, (b) 70% to 90% of PND = effective treatment, (c) 50% to 70% of PND = questionable treatment, and (d) less than 50% of PND = ineffective (Scruggs & Mastropieri, 1998). Trend and variability of data were also analyzed, which is considered a best practice for evaluating results of studies that employ single subject design (Horner, Carre, Halle, McGee, Odom, & Wolery, 2005).

Results:

Overall, comprehension outcomes and instances of positive social interaction increased, while challenging behaviors decreased for targeted students with ASD.

Conclusions:

This poster describes an evidence-based intervention that has demonstrated potential for effectiveness in improving reading comprehension skills, critical for academic success, while also enhancing social skills and reducing challenging behaviors. Whether in the special education or inclusive setting, secondary students with ASD and those that provide them with instruction could benefit from an intervention that meets the unique learning challenges associated with ASD.

**161.182 182** Exploring the Coaching Process and Routine Context of Early Social Interaction (ESI), a Parent-Implemented Intervention for Toddlers with ASD. J. A. Brown*[1], J. Woods[2], R. D. Holland[2], A. M. Wetherby[2] and C. Lord[3], (1)*University of Georgia*, (2)*Florida State University Autism Institute*, (3)*Weill Cornell Medical College*

Background: There is a critical need for systematic measurement and analysis of how parents are taught to use intervention strategies and supports as a part of parent-implemented interventions for young children with ASD. Advancing beyond broad protocol descriptions to data that represents the actual implementation may provide the foundation for examining differential mediating effects of parent-implemented interventions.

Objectives: The purpose of this study was to explore and quantify the caregiver coaching process of the Early Social Interaction Parent-Implemented Intervention (ESI PII). Specifically, coaching behaviors used by interventionists, the caregiver's role in intervention, and the routine context for which intervention was provided were measured in video-recorded intervention sessions across the nine-month home-based intervention.

Methods: Video-recorded home intervention sessions were independently coded in 30-sec intervals for three mutually exclusive and exhaustive coding sets: coaching strategies, caregiver role, and routine context. Initial analysis was completed for 41 interventionist-parent-child triads ($n$=20, Florida; $n$=21, Michigan) across four time points (months 1, 3, 6, & 9). Operationally defined coaching behaviors were categorized as general coaching strategies (conversation and information sharing, observation, joint interaction) and specific strategies (direct teaching and demonstration, guided practice with feedback, caregiver practice with feedback, and problem solving and reflection). The parent's role in intervention was coded as leader, partner, participant, observer/listener, and not present. The routine context was measured across the ESI activity categories of play with toys/objects, play with people, meals and snacks, caregiving, book sharing, and family chores.

Results: Aggregate data analysis demonstrated that the interventionists used a variety of general and specific coaching strategies. The combined strategies of direct teaching and demonstration with narration (10%), guided practice with feedback (12%), and caregiver practice with feedback (12%) represented 34% of the intervention, which is almost double the amount of time spent in conversation and information sharing (18%). Parents demonstrated an active role throughout the the intervention, demonstrated by 75.34% time as partners, 14.05% of time as leaders, and 7.07% of time as participants compared negligible time as observers (1.37%) or not present (1.07%). Majority of the intervention time (77.61%) was comprised of the triads actively participating in a routine (as opposed to planning or reviewing the activity). Within that active participation, the

following routine contexts were proportionally represented: play with toys/objects (39.91%), play with people (7.56%), meals and snacks (16.11%), caregiving (8.08%), book sharing (13.36%), and family chores (1.31%).

Conclusions: The results provide a quantifiable understanding of the process used to teach parents within ESI PII, indicating that interventionists used a combination of coaching strategies that supported the parent in an active role across varied routine contexts to increase their capacity to independently support their child's learning between sessions with the provider. The results provide evidence that ESI PII aligns with the National Research Council (2001) and IDEA Part C recommendations of parent involvement and embedded instruction across meaningful activities. These findings have important implications for extending measurement in parent-implemented interventions to include the process and context used to teach parents.

**161.183 183** Has the Needle Moved for Social Inclusion of Children with ASD? a 10-Year View. L. N. Huynh*[1], Y. C. Chang[1], W. Shih[2] and C. Kasari[3], (1)*UCLA*, (2)*University of California, Los Angeles*, (3)*University of California Los Angeles*

Background:

Developing meaningful relationships is a challenge for children with autism spectrum disorder (ASD). Elementary-age children with ASD have fewer reciprocated friendships and are less engaged with their peers (Kasari et al., 2011). In the past few years, there have been more evidence-based social skills interventions that help children with ASD with social challenges (Kasari & Patterson, 2013). However, little is known about whether the proliferation of social skills interventions has resulted in improved peer relationships for children with ASD at school.

Objectives:

The current study will examine whether there are differences in friendships in cohorts of elementary school-aged children with ASD studied over a ten-year period.

Methods:

Three cohorts of children were studied over a 10-year period, completed a social network and friendship survey regarding their friendships at school. The 3 cohorts were assessed from 2003-2007 (n=60), 2008-2011 (n=115), and 2011-2012 (n=17). Children were fully included in general education classrooms with IQs above 65. There were no significant differences between the cohorts in age, gender, and ethnicity. Participants included 192 elementary children with ASD in the Greater Los Angeles area, ages 6 to 12 ($M$ = 8.31, $SD$ = 1.57); 86% were male. Participants were from diverse ethnic backgrounds (44.3 % Caucasian, 9.2% African American, 17.3% Hispanic, 22.2% Asian, and 7% Other).

The S*ocial Network and Friendship Survey* were used to measure the number of friendships, social centrality, friendship nominations and reciprocity in children with ASD. The *Playground Observation of Peer Engagement* was used to measure engagement with peers on the playgrounds at school.

Results:

A chi-square analysis was used to examine the percentage of reciprocated friendships across the three groups. Approximately 28% of the entire sample had a least one reciprocated friendship; however, there were no differences in the percentage of reciprocated friendships among the three cohorts (21.4 %, 33.7%, 23.5 %), $\chi$ 2 (2, $N$ = 196) =2.908, $p$ =0.234.

One-way ANOVAs were conducted to examine differences in the friendship nominations across the three groups. Children had fewer nominations, both from others and to others, and there were no differences between groups ($F$ (2, 181) = .405, $p$ > .05; $F$ (2, 181) = .831, $p$ >.05).

One-way ANOVAs were conducted to examine how engaged the children were on the playground. There were no differences between groups in the percentage of time children spent isolated (33.6%, 34.5%, 23.3%), ($F$ (2, 181) = 1.118, $p$ > .05) or engaged (40.9%, 41.6%, 48.2%) with their peers, $F$ (2, 181) = .380, $p$ > .05.

Conclusions:

Despite the proliferation of social skills interventions, the current study shows that the situation for children at school remains the same. They are unengaged on the playground and the numbers of nominated friendships remain the same. The numbers of reciprocated friendships

also remain low and stable across all three cohorts. Although there have been much advances in social skills interventions for children with ASD, more work is needed to help children with ASD develop meaningful social relationships in the schools (Kasari & Smith, 2013).

**161.184 184** Improving Hand Function in Adults with Autism Spectrum Disorder and an Intellectual Disability through Participation in an Adapted Physical Exercise Program. K. Carr*, P. McKeen, N. R. Azar, S. Horton and C. A. Sutherland, *University of Windsor*

Background: As the prevalence of autism spectrum disorder (ASD) continues to rise, research specific to adults with ASD, as well as individuals diagnosed with both ASD and an intellectual disability (ID), remains limited. These individuals deserve recognition within the literature as they face distinct challenges, such as impairments in motor control. Recent research suggests that the motor impairments associated with ASD negatively affect participation in recreational and vocational activities and activities of daily living, beyond the impact of any accompanying cognitive impairment. Furthermore, when these motor deficits manifest themselves within the upper extremity (including the hand), they create difficulties in performing adaptive living skills, ultimately limiting independence and quality of life throughout adulthood. Therefore, it is important to develop strategies that mitigate such impairments in motor control, particularly within the hand, as fine motor control is essential to completing activities of daily living.

Objectives: This study sought to examine the change in hand function among a group of adults with ASD-ID following participation in an adapted physical exercise (APEX) program focused on motor skill development.

Methods: Eleven adults with ASD-ID (mean age = 35.5 years, age range = 20-61 years; 2 females) attended an APEX program for 90 minutes twice a week for twelve weeks. All participants engaged in whole body circuit training and practice on fine motor skills. A modified version of the Jebsen Test of Hand Function (JTHF) was administered prior to the program (pre-testing), following 12 training sessions (mid-testing), and following 24 training sessions (post-testing). A faster time to complete the subtests of the JTHF indicated a better performance. Subtest times were the sum of the times achieved for the right and left hand. Linear mixed modeling with compound symmetry repeated covariance structure and a fixed effect of trial (three levels: pre-, mid-, and post-testing) was employed to assess differences in hand function across the three testing periods for each subtest and the JTHF as a whole. Statistical significance was determined at $p \leq 0.05$.

Results: A significant improvement between pre-testing and mid-testing was found for the checker stacking subtest of the JTHF ($p = 0.009$), as well as the total JTHF ($p = 0.023$). Additionally, a significant improvement between pre-testing and post-testing was found for three of the six JTHF subtests (card turning: $p = 0.020$; simulated feeding: $p = 0.025$; checker stacking = 0.024) as well as the total JTHF ($p = 0.010$).

Conclusions: Overall, adult participants with ASD-ID improved their performance on half of the subtests of the JTHF that were administered, as well as performed significantly better on the JTHF as a whole after completing the APEX program. This suggests that adults with ASD-ID who participate in an APEX program focused on motor skill development can experience improvements in various aspects of hand function. The practical importance of these results is far reaching as an improvement in fine motor control may translate into a greater ability to perform adaptive living skills that are required for independence and quality of life among these individuals.

**161.185 185** Predictors of Decreased Dating Anxiety in Young Adults with Autism Spectrum Disorder Following the PEERS® for Young Adults Intervention. J. Sanchez*[1], Y. Bolourian[2], R. Ellingsen[3], K. F. Noorbhai[2] and E. A. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience and Human Behavior*, (2)*The Help Group - UCLA Autism Research Alliance*, (3)*University of California Los Angeles*

**Background:**

Young adults with Autism Spectrum Disorder (ASD) who suffer from core social skill deficits often lack the appropriate behavioral repertoire necessary to interact with others according to social convention; deficits that may affect their ability to develop and maintain meaningful relationships (Rao, Beidel, & Murray, 2008). The Program for the Education and Enrichment of Relational Skills (PEERS®) for Young Adults is a 16-week evidence-based, caregiver-assisted intervention shown to significantly improve social skills knowledge, social responsiveness, and

relationship skills in young adults with ASD (Gantman, Kapp, Orenski, & Laugeson, 2012). In addition to friendship skills, PEERS® for Young Adults also targets skills related to developing and maintaining romantic relationships and decreasing dating anxiety. However, predictors of a treatment outcome related to decreased dating anxiety have yet to be examined.

**Objectives:**

The present study examines the extent to which self-reported empathy, emotion regulation and social skills decreased dating anxiety following the completion of the PEERS® for Young Adults intervention.

**Methods:**

Thirty-eight young adults with ASD ranging from 17-24 years of age (*M*=19.84, *SD*=1.76) participated in weekly 90-minute group treatment sessions for 16-weeks as part of the PEERS® for Young Adults program. To assess treatment outcome, young adult participants completed pre and post-treatment measures including the Dating Anxiety Scale (DAS; Glickman & La Greca, 2004). In order to assess predictors of decreased dating anxiety following treatment, baseline measures were examined, including young adult self-reports on the Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004), Social Skills Inventory (SSI; Riggio, 1986), and the Difficulties in Emotional Regulation Scale (DERS; Gratz & Roemer, 2004). Pearson correlation coefficients were calculated to understand the relationships between baseline functioning and decreased dating anxiety following treatment.

**Results:**

Results suggest that dating anxiety decreased in young adult participants following treatment ($p<.05$). Further, results indicate that baseline young adult-reported emotional and social communication skills on the SSI ($p<.05$), awareness and understanding of emotions on the DERS ($p<.10$), and empathy on the EQ ($p<.10$) predict greater decrease in dating anxiety over the course of the intervention.

**Conclusions:**

These findings suggest that upon entry into treatment, young adults with ASD with better self-reported emotional and social communication skills, greater awareness and understanding of emotions, and higher empathic abilities are more likely to decrease in their dating anxiety over the course of the PEERS® for Young Adults intervention. These findings are important because they provide useful information about who may be more likely to benefit from targeted treatment to decrease dating anxiety in young adults with ASD.

**161.186 186** Social Outcomes of a Fundamental Motor Skill Intervention for 4 Year Old Children with Autism Spectrum Disorder. E. Bremer* and M. Lloyd, *University of Ontario Institute of Technology*

Background: Children with Autism Spectrum Disorder (ASD) experience delays in their social interactions and communication skills; however, they also experience significant delays in fundamental motor skill proficiency. Active play is a critical component in the development of young children as it provides an opportunity for the development of social, communication, and motor skills. We propose that a low level of motor proficiency in children with ASD may inhibit their ability to engage in active play; thus, further limiting their opportunities for the development of social and communication skills.

Objectives: The purpose of this study was to investigate whether a fundamental motor skill intervention was effective in improving the social and communication skills of 4 year old children with ASD. A secondary objective was to determine whether the intensity of the motor skill intervention had an impact on social and communication outcomes.

Methods: Nine children that were 4 years of age with ASD participated in this study. Participants were assigned to one of two groups: Group 1 received the motor skill intervention for 1 hour per week for 12 weeks; Group 2 received the motor skill intervention for 2 hours per week for 6 weeks. Sessions focused on teaching fundamental motor skills (running, jumping, throwing, etc.) through direct instruction, active games, and free play. Social behaviour was assessed with the Vineland Adaptive Behavior Scales-2 (VABS-2). Parents completed the VABS-2 pre- and post-intervention, as well as at a 6-week follow-up. An analysis of variance with repeated measures was used to examine changes in social behaviour across the three assessments, as well as

investigate group by time interactions. Participant scores were also examined for individual changes.

Results: Six participants returned their questionnaires at all three assessments and were included in this analysis. Individual gains in social behaviour were found across all variables. Group receptive communication raw scores remained the same from pre- to post-intervention but, improved at the 6 week follow-up (from 26.67 to 30.00), which was not statistically significant ($F(2,10) = 3.195$, $p = 0.085$). Personal care raw scores improved from pre- to post-intervention (41.33 to 46.67) and improved further at the 6 week follow-up to 49.33, which was statistically significant ($F(1.064,5.322) = 8.566$, $p = 0.030$). The adaptive behavior complex percentile score improved from 14.83% to 20.17% and further to 22.00% from pre- to post- to follow-up, respectively ($F(2,10) = 3.376$, $p = 0.076$). No group by time interactions were found on any of the social variables, indicating that there was no difference in intervention intensity on social improvement.

Conclusions: Results from this preliminary study indicate that functional gains in social and communication skills can be made for young children with ASD through a fundamental motor skill intervention. Practitioners are encouraged to employ similar motor skill programs in order to intervene on both the motor and social deficits experienced by young children with ASD. These results warrant further research with a larger sample.

**161.187 187** Teaching Playground Staff at Schools to Improve Peer Engagement for Children with Autism Spectrum Disorders. M. Kretzmann*, W. Shih and C. Kasari, *UCLA*

Background: Children diagnosed with autism spectrum disorder (ASD) often experience difficulties engaging with typically developing peers in the general education setting. Well-meaning school personnel can further complicate outcomes by following intuitive intervention strategies targeting a specific child when, at times, simple strategies providing all children with a better social environment at recess could produce better results for children with ASD.

Objectives: As part of a continuing effort to help improve peer engagement for children with ASD, we aimed to test a new, more naturalistic approach to intervention within the general education setting. We wanted to show that school personnel could easily improve key elements of the social lives of children with ASD during recess.

Methods: Using a randomized, wait-list-controlled design, a psychosocial intervention was taught to 35 school personnel and delivered to children with ASD during recess at four elementary schools. The immediate treatment (IT) group consisted of 13 (two female) elementary school students with ASD and the wait-list (WL) group contained 11 (four female) students with ASD. The intervention aimed to 1) increase the ability of playground aides to facilitate peer engagement, and 2) increase joint engagement with peers for children with ASD.

Results: Responsive behavior scores by the adults showed significant improvement over time for the IT group compared to the WL group, ($F(1,173)=6.83$, $p=0.01$). The treatment effect was not maintained as the IT group did not make significant gains by follow-up compared to its entry ($F(1,55)=6.76$, $p=0.99$).

The percentage of strategic behavior use scores were not significantly different between the IT and WL groups although there was a trend for the immediate treatment group to show more of these behaviors ($F(1,173)=3.09$, $p=0.08$). The percentage of strategic behaviors usedby group were also not significantly different by follow-up compared to entry ($F(1,55)=0.1$, $p=0.75$)).

Some of the adults were one-on-one aides (n=5), and some were assigned to supervise the entire group of children on their respective playgrounds (n= 30). At entry one-on-one aides displayed significantly lower responsive and strategic behaviors than regular playground staff; responsive behaviors ($F(1,173)=3.55$; $p=0.06$) and strategic behaviors ($F(1,173)=9.51$; $p=0.002$). Both one-on-one and playground staff increased strategic behaviors from entry to exit ($F(1,173)=15.44$; $p=0.001$). The rate of improvements were significant across groups ($F(1,173)=5.46$; $p=0.02$) with one-on-one staff having better improvements from entry to exit. Also both one-on-one and playground staff increased responsive behaviors from entry to exit ($F(1,173)=8.9$; $p=0.003$). The rate of improvements were not significant across groups for responsive behaviors ($F(1,173)=1,09$; $p=0.30$).

There was a significant treatment by time effect with children in the IT groups rated as more engaged with peers on the playground than children in the WL groups from entry to end of treatment ($F(1,108)=10.68$, $p=0.002$). In a separate analysis, the effect of treatment for the IT groups was maintained at the follow up ($F(1,35)=6.76$, $p=0.014$).

Conclusions: Results suggest that a low dose, brief intervention delivered by playground staff can be beneficial in jumpstarting peer engagement for children with autism in inclusive settings, but ongoing support of playground staff is likely needed.

**161.188 188** The Impact of Participant Characteristics on the Effectiveness of Facial Emotion Training in Children with Autism Spectrum Disorders. J. K. Johnson*, B. Evans-Smith and N. M. Russo-Ponsaran, *Rush University Medical Center*

Background: Struggling to identify emotions from facial expressions can have a detrimental impact on a child's social development and future success. Individuals with autism spectrum disorders (ASD) often fail to notice the emotions of those around them. Targeted interventions have been shown to improve the ability of children with ASD to recognize emotions from facial expressions.

Objectives: The primary aim of this study is to evaluate how participant characteristics impact the effectiveness of facial emotion training in children with ASD. Specifically, we were interested in evaluating how pre-training facial emotion recognition skill, intellectual ability, age or autism severity impact the success of a coach-assisted, computer-based facial emotion training intervention. The intervention included didactic instructional videos of adults demonstrating seven basic emotions (happy, sad, angry, disgust, fear, surprise, and contempt), repeated practice, imitation exercises and a post-session assessment. Screen modifications directing children to important changes in facial features (eyes, eyebrows, and mouth) were also utilized during training.

Methods: Children with ASD were pre-screened for eligibility based on age, average intellectual ability (WASI-II; IQ ≥ 80), autism status (based on history of diagnosis, SCQ, ADI-R, and ADOS scores) and facial emotion recognition deficit (based on several direct assessments including the MiX, DANVA, and CATS). Once determined eligible, a block randomization design was used to assign participants to either a wait-list control (WLC) or active intervention (AI) group. Twenty-four children with ASD (12=WLC; 12=AI; ages 8-15 years) participated. Children in the AI group participated in one-hour treatment sessions twice weekly until s/he reached a set criterion. Upon completing training, children in the AI group completed an assessment battery of direct and indirect facial emotion recognition assessments and general social functioning. Participants assigned to the WLC group followed the same assessment schedule, but received the intervention following the completion of outcome measures. ANCOVAs were used to analyze the effects of pre-training facial emotion recognition skill, intellectual ability, age and autism severity on outcomes.

Results: Children in the AI group improved in their facial emotion recognition. Data showed that the impact of the intervention on post-training facial emotion recognition skill was different at different levels of children's pre-training skill. Specifically, the intervention had statistically significant effects on post-training MiX scores in participants with lower pre-training MiX ($F(1,18)=9.809$, $p=.006$) and DANVA scores ($F(1,17)=6.300$, $p=.022$). There were no significant effects of intellectual ability, age or autism severity on the impact of the intervention.

Conclusions: These data support that the more severe the facial emotion recognition deficit, the greater the impact of facial emotion recognition training. That there were no effects of intelligence, age or autism severity on the results may indicate that children of a broader range of ability may be equally successful after training. Further analyses will be conducted to explore other potential contributors to the success of facial emotion recognition training.

**161.189 189** The Role of Pragmatic Speech in the Effectiveness of an Anxiety-Focused Cognitive Behavior Therapy for Adolescents with Autism Spectrum Disorders. A. Trubanova*, R. Elias and S. W. White, *Virginia Polytechnic Institute and State University*

Background:

Many children and adolescents with autism spectrum disorder (ASD) face communication challenges in everyday social interactions. While language and communication impairments have

been assessed through semantic, syntax, and morphology domains in children with ASD, few studies have looked into pragmatic aspects of speech and how the challenges in pragmatic speech may affect treatment progress. Pragmatic domain of language focuses on the social aspects of language and communication which is often impaired in individuals with ASD. Therefore, it is important to consider the role of pragmatic speech when evaluating the effectiveness of many cognitive behavioral treatments that aim to address the social difficulties of individuals with ASD and anxiety.

Objectives:

The goal of the current project is to investigate whether assessed pragmatic speech ability is associated with treatment response following brief cognitive behavioral therapy targeting anxiety and social competence.

Methods:

Pragmatic speech was evaluated in adolescents with ASD and at least one anxiety disorder using the Children's Communication Checklist-2 (CCC-2; Bishop, 2003), a parent questionnaire used to assess pragmatic communication. Participants were randomly assigned to two conditions: 15 of the individuals received a 14-week cognitive-behavioral treatment program for anxiety and social skills (Multimodal Anxiety and Social Skills Intervention for Adolescents: MASSI) and 15 of the individuals were assigned to a waitlist condition. CCC-2 and the Multidimensional Anxiety Scale for Children (MASC; March, 1997), a measure of anxiety symptoms, were collected at baseline and at the end of the 14-week trial.

Results:

Results from the participants with complete data (n = 15 for treatment; n = 12 for waitlist condition) show that while General Communication Composite (GCC) score was not related to amount of anxiety reported at baseline by the adolescents on the MASC (r = .122, p = .544), communication skills were found to be correlated with a reduction of anxiety symptoms between baseline and endpoint of the study for the treatment group only (r = .539, p = .038). Specifically, greater deficits in communication skills at baseline predicted a reduction of anxiety symptoms from pre-treatment to post-treatment. This effect was found only for self-report, not the parent report, of change in anxiety symptoms.

Conclusions:

Overall, this study suggests that pragmatic speech predicts self-reported anxiety reduction in adolescents with ASD who receive cognitive-behavioral treatment for anxiety and social skills. This finding provides support for a relationship between ASD severity and anxiety, in that severity of ASD as assessed by deficits in social communication, is predictive of improvement with treatment. In addition, since communication skills predicted self-reported change in anxiety, but not parent-reported change in anxiety, this study highlights an important distinction between self-report and parent-report of anxiety in adolescents with ASD. Lastly, these findings highlight the importance of exploring facets of social communication, in addition to semantic, syntax, and morphology aspects, that are a factor in response to cognitive-behavioral treatment for ASD and anxiety.

**161.190 190** The Use of Mobile Technology in the Treatment of Prosodic Deficits in Autism Spectrum Disorders. E. Schoen Simmons*[1], C. A. Wall[1], R. Paul[2] and F. Shic[1], (1)*Yale University School of Medicine*, (2)*Sacred Heart University*

Background: Language deficits in ASD are both highly prevalent and have significant impact on adaptive functioning. For 80% of individuals with ASDs who acquire spoken language, deficits in prosody are among the most chronic impairments. Prosodic speech deficits impede social interaction and limit participation in daily activities. Despite the handicapping nature of prosodic disorders, there are few interventions to treat these deficits.

Objectives: The purpose of this study is to assess the feasibility and preliminary utility of an application, *SpeechPrompts,* for iOS devices in the treatment of prosodic disorders in school-age children with ASD.

Methods: Students, 5-19 years of age with a diagnosis of ASD and prosody deficits, were enrolled in the study (N=40). These students were recruited from the caseloads of school-based speech-language pathologists (SLPs; N=10) in an educational setting. SLPs recorded speech samples for each student pre and post intervention. These samples were rated by an SLP

unfamiliar with the students using a Likert scale for each of the following prosodic features: Rate, Rhythm, Intensity, Stress, Global Intonation. *SpeechPrompts* is an iOS application whose main function is to provide a visual representation of the prosodic features of speech. The application provides both real-time feedback and opportunities for the student to match their speech to an adult or peer target. Each SLP received an iPad with the *SpeechPrompts* application. A brief tutorial was provided to each SLP and included instruction on the use of the main features of the application. The application was presented to the enrolled students as part of their speech and language services. The SLPs were instructed to use the application as them deemed fit using clinical judgment. Intervention duration was ten weeks. SLPs completed weekly engagement questionnaires for each of their students which rated the students' and SLPs' experiences with *SpeechPrompts*. SLPs also completed end-of-study surveys.

Results: Usage data collected revealed SLPs accessed the application daily during the school week with a median frequency of 2.5 sessions per day. Post-treatment prosody ratings based on speech samples obtained at end of treatment indicated improvements in prosodic functioning with greatest improvements observed in vocal intensity and stress patterns. Engagement measures indicated that students enjoyed the sessions (88%), did not engage in disruptive behavior while using the application (88%) and looked forward to using the application again (96%). All SLPs enrolled in the study reported that they felt comfortable recommending *SpeechPrompts* to colleagues in end-of-study surveys.

Conclusions: Results of this study suggest that *SpeechPrompts* has the potential to be a useful tool in the treatment of prosodic disorders as seen by improvement in prosodic functioning in this small group of students. Moreover, the application appears to maintain the student's attention and engagement over the course of treatment. In conclusion, *SpeechPrompts* provides SLPs with an additional tool in their repertoire to address these difficult to treat set of speech difficulties commonly observed in children with ASDs.

**161.191 191** Well-Being in a Novel Cultural Milieu: Examining the Well-Being of Mothers of Children with Autism in Lebanon.

R. Obeid*[1] and N. Daou[2], (1)*The Graduate Center - CUNY*, (2)*American University of Beirut*

**Background:** Research in the Western world has shown that mothers of children with autism typically display lower levels of well-being compared to mothers of typically developing children and children with other disabilities (Hastings, 2008). Multiple factors affect such decreased well-being, the coping style used plays a critical role in the well-being of mothers of children with autism (Benson, 2008). Across cultures, social support has been regarded as an essential buffer in the face of stress (Benson, 2010). Compared to all other symptoms in autism, behavioral symptoms are mostly associated with decreased well-being levels (Lin et al., 2010). Lebanon is a country where parents of children with autism do not receive adequate financial or educational support from the government, additionally, stigma for the disabled and their families remains high in the population. Thus, parents need to rely on their surroundings and their own financial status to take care of their child with a disability, which can be very costly.

**Objectives:** This study examined the extent to which coping style, child's behavioral problems, and perceived social support impact the well-being of mothers of children with autism in Lebanese mothers, thus making this study a first of its kind in the region. The well-being of mothers of children with autism was also compared to that of mothers of children without an autism diagnosis in this novel cultural milieu.

**Methods:** A total of 161 mothers took part in this study. The sample consisted of 65 mothers of children with autism and 98 mothers of children without autism. All mothers of children with autism answered questionnaires related to coping strategies they use while dealing with their child's diagnosis, their child's level of behavioral problems, their perceived social support, and their overall well-being. Mothers in the non-autism group only responded to questionnaires related to their well-being.

**Results:** Results of multiple regression analyses showed that disengagement and distraction coping were the only variables that predicted well-being among mothers of children with autism. In terms of correlational analyses, Cognitive reframing, disengagement and distraction coping, in addition to the child's behavioral problems,

were all correlated with well-being. Social support variables did not correlate with well-being in this sample. Finally, significant differences in well-being were observed between mothers of children with autism and mothers of children without an autism diagnosis.

**Conclusions:** Individual and cultural differences play a critical role in how parents respond to challenges related to their child's diagnosis. This study showed that the effects of engagement, distraction,and cognitive reframing in a Lebanese sample paralleled research conducted in the Western world. The majority of mothers reported using problem-focused coping strategies more than emotion-focused strategies, which were found to predict well-being. The most unexpected finding of the present study was that perceived social support did not significantly predict well-being. This is inconsistent with what the literature has reported regarding social support variables in multiple cultures (Lin et al., 2010),this might be due to the fact that social support while raising any child is a given in most families in Lebanon.

## 162 Autism Social, Legal and Ethical Research

Co-Chairs: Liz Pellicano, PhD (Institute of Education, Univ. of London); Michael Yudell, PhD (Drexel Univ. School of Public Health) Bryna Siegel, PhD (Autism Center of N. Calif. & UCSF) Political & Ethical Considerations in Autism Research and Treatment. The 3rd year of this SIG will explore social, ethical and legal issues concerning autism research and treatment, particularly how these impact the needs of less able individuals who are or will soon become adults. Speakers will include: • Dr. Bryna Siegel • Dr. Deborah Barnbaum • Dr. Carolyn Klebanoff • John Elder Robison will act as Discussant

## 163 Minimally Verbal Individuals

Co-Chairs: Nancy Jones, PhD, Terry Katz, PhD, Connie Kasari, PhD The goal for 2014 is to develop practice parameters for minimally verbal individuals (MVI) in the areas of: characterization, evaluation, intervention, developmental considerations and underserved populations. We will facilitate mentorship partnerships within the projects. Specific aims include: 1) Provide a brief review of current literature 2) Workgroups will: a. Discuss the current literature and identify critical gaps b. Outline plans for the development of one or two specific practice parameters c. Establish the project goals and key milestones, aiming to present at IMFAR 2015. d. Leaders will organize project teams with mentors partnered with junior faculty and student members.

## 164 Sensory Motor Special Interest Group (SMIG)

Co-chairs: Alison Lane (University of Newcastle, Australia) and Justin Williams (University of Aberdeen, Scotland) Our goal for 2014-2015 is to foster collaboration between sensory and motor researchers. The Sensorimotor Interest Group (SMIG) was formed from 2 separate sensory and motor special interest groups. Hence, participants tend to have a primary interest in either sensory or motoric aspects of autism. However, motoric and sensory problems are closely related, and indeed, we consider that impaired sensori-motor integration is a core developmental impairment in autism. As such, the next generation of researchers in this field will likely spend considerable time in their careers exploring these questions. We consider that a valuable function of our group is to promote and facilitate research, which can further explore the relationship between motor and sensory problems.

## 165 Keynote Address

Keynote Address - Saturday

**165.001** The Development of Attention: Implications for Early Identification. J. Colombo*, *University of Kansas*

## 166 Brain Function and Structure II

*Organizer:* C. Ecker *Institute of Psychiatry, King's College London*

**166.001** Auditory Gamma-Band Power Is Related to GABA Concentration in Autism. D. C. Rojas*[1], S. Steinmetz[2], S. L. Hepburn[3] and M. S. Brown[4], (1)*University of Colorado Denver Anschutz Medical Campus*, (2)*University of Colorado Denver*, (3)*JFK Partners/University of Colorado School of Medicine*, (4)*University of Colorado Anschutz Medical Campus*

Background:

Gamma band oscillatory activity, as measured using EEG and magnetoencephalography (MEG), has been associated with intrinsic GABA in animal models and in combined MR spectroscopy and MEG studies. We have previously published data demonstrating that auditory gamma-band responses are reduced in people with autism and their first-degree relatives, suggesting the utility of some of the findings as endophenotypes. Independently, prior work has suggested elevation of reduction of GABA in persons with autism. The relationship between GABA concentration and auditory gamma-band activity has not yet been studied in autism.

Objectives:

To assess the relationship between auditory GABA concentration and auditory gamma-band power in individuals with autism, unaffected siblings of persons with autism, and in control subjects.

Methods:

We examined auditory transient and steady-state gamma-band responsesand auditory cortical GABA concentration in 3 groups of children and adolescents: a) healthy controls (N=25), b) people with autism spectrum disorders (N=24) and c) unaffected siblings (N=19) of older children with ASD. Auditory response data were acquired using a 248-channel magnetoencephalography (MEG) system, and glutamate concentrations were obtained from proton magnetic resonance spectroscopy (1H-MRS) using a MEGA-PRESS sequence on a 3T MRI system. All measures were restricted to the left hemisphere due to time constraints of the spectroscopy sequence.

Results:

Transient gamma-band power was significantly higher in the control group compared to individuals with autism ($p < .01$) and the sibling group ($p < .05$). Auditory steady-state gamma-band power was also higher in controls than in the autism and sibling groups. GABA concentration was significantly lower in the autism ($p < .05$) and sibling groups ($p < .05$) compared with controls. GABA concentration was correlated with transient gamma-band power in the control group ($r = .45$, $p < .002$). In the autism group, the association between GABA and gamma-band power approached significance, $r = .35$, $p = .08$. The sibling group also exhibited a significant association between GABA concentration and gamma-band power, $r = .51$, $p = .02$. No correlations with steady-state response power and GABA were observed.

Conclusions:

This study suggests that reduced GABA concentration might be related to reductions in stimulus related gamma-band power that have frequently been reported in autism. The fact that only the obligatory transient auditory gamma response was associated with GABA levels implicates different mechanisms of generation for the transient and steady-state responses, consistent with earlier literature suggesting that the steady-state responses reflect superimposition of mid-latency auditory evoked responses. GABA concentration and gamma-band power may both be related endophenotypes in autism that are related to an underlying change inhibitory function.

**166.002** Abnormalities in Subcortical Glutamate/Glutamine, but Not GABA, in Adults with an ASD: A [1H]MRS Study. M. A. Mendez*, J. Horder, N. Gillan, S. Coghlan and D. G. Murphy, *Institute of Psychiatry, King's College London*

Background: A major emerging hypothesis is that abnormalities in brain function in people with ASD are underpinned by abnormalities in the balance of inhibitory GABA and excitatory glutamate neurotransmission. This excitatory:inhibitory imbalance theory is indirectly supported by animal, postmortem and electrophysiological evidence - and we previously reported pilot evidence that adults with ASD have a significant reduction in glutamate/glutamine concentration in the basal ganglia. However, nobody has yet measured GABA in adults with ASD, or probed whether neurochemical abnormalities (in glutamate/GABA) are associated with abnormal patterns of neural function.

Objectives: For the first time in adults with ASD, we used proton MEGAPRESS magnetic resonance spectroscopy ([1H]MRS) together with resting state fMRI to quantify (respectively) both GABA and glutamate, and the functional connectivity of left basal ganglia, in medication free adults with ASD.

Methods: We recruited 54 right-handed adult (age 18+) male participants: 24 individuals with ASD and 30 healthy controls who were well matched for age, gender and IQ. All participants had an IQ above 80. Participants in the ASD group met ICD-10 and ADOS-G/ADI-R criteria for autism spectrum disorder. The two groups did not differ in age (t-test, $p=0.23$) or full-scale IQ ($p=0.33$). Basal ganglia MEGAPRESS was acquired on a 3 Tesla General Electric MRI scanner using a single voxel centred on the left putamen. Absolute metabolite concentrations were determined using LCModel 6-3-0I software, with water scaling, and corrected for voxel CSF composition. We acquired resting state functional MRI (rsfMRI) in the same scanning session (EPI, TR=2 seconds, 256 volumes). rsfMRI data were analyzed using FSL software (v 4.1.8) Following preprocessing, we calculated seed-voxel connectivity maps for each participant using a seed ROI placed in the left putamen.

Results: Adults with ASD had a significant reduction in the Glx (glutamate and glutamine) signal (p=0.033) as compared to controls. However, there were no significant group differences in BG levels of GABA (two-tailed t-test: p=0.39) or in the glutamate:GABA ratio. Lower Glx was associated with more severe symptoms on the ADOS Social impairments domain. Further, we confirmed the functional relevance of the glutamate/glutamine reduction by integrating this finding with rsfMRI. We found that basal ganglia Glx was positively correlated with the degree of connectivity between the putamen and a network of cortical areas ($p<0.05$ whole brain cluster corrected). Further, the Glx-connectivity association was stronger ($p<0.05$ whole brain cluster corrected) for healthy controls than for ASD patients in medial frontal and superior temporal lobe.

Conclusions: This study replicates (in a different sample) previous findings from our laboratory (Horder et al 2013) that adults with ASD have a significant reduction in basal ganglia glutamate/glutamine. Further, we now demonstrate that these differences in glutamate/glutamine are associated with abnormal 'baseline' brain functional connectivity, and severity of clinical symptoms.

**166.004** Empathy in ASD: Using ERPs to Identify Atypical Neural Responses to Physical and Social Pain. E. J. Levy*[1], C. E. Mukerji[1], A. Naples[1], R. Bernier[2], R. Tillman[1], H. S. Reuman[1], J. H. Foss-Feig[1], D. Perszyk[3] and J. McPartland[1], (1)*Yale University*, (2)*University of Washington*, (3)*Northwestern University*

Background: Neuroimaging studies have revealed specific brain systems subserving empathic processing. Research in typical development (TD) indicates that observed physical and social pain evoke distinct affective and cognitive empathic responses in neural circuitry. Our prior work in TD revealed event-related potential (ERP) biomarkers for empathic processing: a rapid negative peak (N110) and a later positive deflection (P3) were associated with affective sharing and cognitive evaluation of pain, respectively. In addition, these biomarkers were modulated by autistic traits. The current research applies these findings to autism spectrum disorder (ASD) and investigates, for the first time, mu wave suppression, an index of mirror neuron system function, as a marker of empathic response to social pain.

Objectives: Using EEG and ERPs, the current study aims to: (i) differentiate the temporal dynamics of brain response to physical and social pain in TD and ASD adults; (ii) examine group differences in suppression of mu wave activity in response to observing others' pain; and (iii) identify relationships among empathic characteristics, social functioning, and neural response to observed social pain. We predicted atypical embodied and cognitive empathic responses to both physical and social pain in ASD, reflected in changes in N110 and P3 responses. In addition, we expected attenuated mu suppression in ASD relative to TD. We hypothesized that trait empathy and social functioning would correlate with neural response to social pain.

Methods: Participants were 20 adult males with ASD and 20 age-matched TD adult males. EEG was recorded with a 128-electrode Hydrocel Geodesic Sensor net. Participants viewed dynamic and static images of social versus physical pain presented in four counter-balanced blocks; attention to pain was manipulated with an empathic versus distractor task. In each block, 50% of stimuli were painful and 50% were analogous but painless. Empathic traits and social functioning were measured using the Empathy Quotient (EQ) and Social Responsiveness Scale Adult Self-Report (SRS-A-SR). ERPs and oscillatory EEG activity were extracted for each condition at central leads (C3/C4).

Results: ERP results indicated (i) increased N110 amplitude in response to painless stimuli in ASD compared to TD ($p$=.001), (ii) marginally longer right hemisphere P3 latency in response to social versus physical pain in ASD ($p$=.059) but not in TD ($p$>.05), and (iii) shorter right hemisphere P3 latency to physically painful stimuli in ASD versus TD ($p$=.012). Greater amplitudes to social versus physical pain at N110 and at P3 correlated with increased social responsiveness within the ASD population and trait empathy across groups ($p$s=.030 and .002, respectively).

Conclusions: Individuals with ASD display distinct brain responses to social versus painful stimuli relative to TD counterparts. These differences were evident in neural markers of both affective and cognitive empathic responses. Notable differences were also observed in neural response to social and physical pain between groups; these changes correlated with empathic traits, which

were characteristically diminished in ASD. The present results help to explain variability in social empathic behavior in ASD and inform targeted intervention strategies focused on affective response versus cognitive awareness of social pain.

**166.005** Neural Responsivity to Tactile and Auditory Sensory Stimuli in Youth with and without ASD. S. Green*[1], D. Beck-Pancer[1], L. M. Hernandez[2], J. J. Wood[3], J. D. Rudie[4], M. Dapretto[1] and S. Y. Bookheimer[1], (1)*UCLA*, (2)*University of California, Los Angeles*, (3)*University of California Los Angeles*, (4)*Ahmanson-Lovelace Brain Mapping Center, UCLA*

**Background:** Children with ASD often exhibit sensory over-responsivity (SOR), which may cause them to react negatively to sensory stimuli such as noisy environments or scratchy clothing (Liss et al., 2006). Rates of SOR are over five times higher in children with ASD than in typically developing (TD) children (e.g., Baranek et al., 2006; Ben-Sasson et al., 2007) and SOR is associated with increased functional impairment in children with ASD (e.g., Liss et al., 2006; Pfeiffer et al., 2005). Results from a prior study from our lab examining fMRI responses to visual and auditory stimuli suggest that hyperactivation in the limbic system, primary sensory cortices, and prefrontal cortex is associated with higher SOR symptoms (Green et al, in press). The present study extends our early findings by examining fMRI responses to tactile and auditory stimuli in youth with and without ASD.

**Objectives:** 1) To examine differences in brain responses to auditory and tactile stimuli in youth with and without ASD; 2) To examine the relationship between parent- and child-reported SOR symptoms and brain responses to sensory stimuli; and 3) To examine functional connectivity during exposure to sensory stimuli.

**Methods:** Participants were 16 children and adolescents with ASD and 16 TD matched controls, between 8-17 years. During fMRI, participants were presented with mildly aversive auditory stimuli (noisy traffic sounds) and tactile stimuli (scratchy sweater rubbed from wrist to elbow). The block design paradigm included 4, 15-sec trials of each stimulus type: the auditory stimulus, tactile stimulus, or both. Participants' parents rated their symptoms of SOR with the Short Sensory Profile (Dunn, 1999). Scores on the relevant subscales (auditory and tactile sensitivity) were standardized and combined to create a sensory composite score. Parents also rated their children's anxiety symptoms using the SCARED.

**Results:** FSL was used to run subject-level and then group-level analyses. Within- and between-group analyses were thresholded at $Z>2.3$ ($p<.01$). The ASD group showed greater activation in amygdala, hippocampus, thalamus, striatum, orbital frontal cortex, and somatosensory cortex. A regression model was used to predict fMRI response within both groups from SOR scores, controlling for anxiety. The same areas were significantly related to SOR score in both groups. Additional analyses examine functional connectivity with the amygdala as a seed region.

**Conclusions:** In one of the first fMRI studies of tactile stimulation with children with ASD, we confirm prior findings that SOR is related to hyperactivation of the limbic system and primary sensory cortices. Functional connectivity between amygdala and striatum, orbital frontal cortex, and somatosensory cortex is also discussed.

**166.006** Reward Anticipation and Processing of Social Versus Nonsocial Stimuli in Children with and without Autism Spectrum Disorders. K. K. Stavropoulos* and L. J. Carver, *University of California, San Diego*

**Background:** How children respond to social and nonsocial rewards has important implications for understanding both typical and atypical social cognitive development. Individuals with autism spectrum disorders are thought to process rewards differently than typically developing individuals. Specifically, previous theories suggest that children with autism may have less motivation to engage in social interactions because social stimuli are not rewarding. However, there is little direct evidence to support this claim, and previous studies have not controlled for reward or stimulus properties.

**Objectives:** The current study was designed to measure reward anticipation and processing in children with and without autism while controlling for both reward and stimulus properties. We wished to clarify whether children with autism demonstrated deficits in reward anticipation and processing to both social and nonsocial stimuli, or whether these deficits were confined to social stimuli only.

**Methods**: We utilized event-related potentials (the stimulus-preceding negativity, SPN and feedback-related negativity, FRN) to measure differences in reward anticipation and processing during a guessing game in 6-10-year-olds with (*N* = 20) and without (*N* = 23) a diagnosis of autism. Children were presented with reward indicators accompanied by incidental face or non-face stimuli. Non-face stimuli were comprised of scrambled faces in the shape of arrows, controlling for low level properties of the two conditions.

**Results:** Children with autism showed significantly smaller responses while both anticipating and processing social rewards compared to typically developing children. However, reward anticipation and processing on nonsocial rewards was intact. Correlations between severity of autism symptomology and brain activity measures suggested that children who experienced more reward anticipation for nonsocial stimuli had more severe autism symptoms.

**Conclusions:** While typically developing children find a face stimulus more rewarding than a non-face stimulus, children with autism do not. This is the first study to measure both reward anticipation and processing in children with and without autism while controlling for reward properties across conditions. These findings provide evidence that children with autism have reward anticipation and processing deficits for social stimuli only, rather than global reward deficits. Further, while our electrophysiological results suggest a lack of reward value to social stimuli in autism, our correlational findings reveal that perhaps children who are overly rewarded by nonsocial stimuli have more severe symptoms of autism. Thus, it might be the case that an overabundance of nonsocial motivation may occur at the expense of social motivation in children with autism.

**166.007** Sex Differences in Brain Structure of Preschool-Aged Children with Autism Spectrum Disorder. C. W. Nordahl*[1], F. Hoeft[2], H. Ota[3], A. Lee[4], S. J. Rogers[4], S. Ozonoff[4] and D. G. Amaral[4], (1)*UC Davis MIND Institute*, (2)*University of California at San Francisco*, (3)*Showa University School of Medicine*, (4)*University of California Davis Medical Center*

Background: Autism spectrum disorder (ASD) affects 1 in 88 children in the United States, but the disorder is much more common in boys than in girls. Although this disparate sex ratio is among the most highly replicated findings in studies of ASD, sex differences in the neuropathology of ASD remain poorly understood, particularly in young children. Normative brain development is sexually dimorphic, but we do not yet know how biological sex affects the developing brain in ASD.

Objectives: We evaluated within- and between-sex differences in cortical gray matter volumes in a large cohort of preschool-aged children with ASD and age-matched typically developing controls.

Methods: We acquired structural T1-weighted MRIs in 174 children with ASD (140 male, 34 female) and 90 age-matched typically developing (TD) controls (59 male, 31 female). Mean age at time of MRI acquisition was 37 months. Cortical gray matter volumes, parcellated into 34 gyral regions in each hemisphere, were obtained through Freesurfer v5.1.0. The automated processing stream includes motion correction of MRI image, removal of non-brain tissue, transformation to Talairach space and intensity normalization. We utilized multivariate pattern analysis to identify patterns of brain regions that discriminate between sex and diagnosis. We performed cross-validated linear support vector machine (SVM) analyses controlling for total gray matter volume and age for the following comparisons: ASDf v TDf, ASDm v TDm, ASDf v ASDm, TDf v TDm, and ASD v TD (with sex as additional covariate). We also recursively selected features that contributed the greatest weights for the classifications by performing t-tests (alpha = 0.1). All steps were performed iteratively using training sets (not including test set) to remain unbiased and avoid overgeneralization. We report: (1) classification accuracy of test sets, (2) feature weights that contributed to the classification, and (3) the overlap and non-overlap in brain regions across different comparisons.

Results: Our preliminary results from a subset of the full sample (156 ASD, 77 TD) suggest that classification accuracy was greatest for the ASDf v ASDm comparison (86%) suggesting that male and females with ASD do indeed have distinct patterns of neuropathology. Accuracy for all other comparisons ranged from 65-70%. For the within sex comparisons (ASDf v TDf and ASDm v TDm), the only overlapping region is left superior temporal gyrus, a region that has been widely

implicated in ASD and has many functions, including semantic language processing and social communication. Regions specific to the ASDf v TDf comparison included regions in neural systems related to understanding mental states of others (right temporal pole) expressive language and reception of facial communication (bilateral pars opercularis, cingulate gyrus) as well as right postcentral gyrus, right superior frontal gyrus, and left transverse temporal gyrus. Interestingly, two of these regions, right temporal pole and right pars opercularis were also sexually dimorphic in typically developing controls (TDf v TDm) comparisons.

Conclusions: These data suggest that females and males with ASD have patterns of neural abnormalities that are more dissimilar than similar.

**166.008** White Matter Microstructure in Girls with Autism Spectrum Disorder: Comparison with Neurotypical Controls and Unaffected Siblings. R. J. Jou*[1], C. R. Gibbard[1], C. M. Pretzsch[1], D. Yang[1], I. Y. Murphy[1] and K. A. Pelphrey[2], (1)*Yale Child Study Center, Yale School of Medicine*, (2)*Yale University*

Background:

Studies implementing tract-based spatial statistics (TBSS) in samples consisting mainly of boys have shown abnormalities in white matter (WM) microstructure in autism spectrum disorder (ASD). One such study reported similar WM abnormalities in unaffected sibling (US) and ASD groups, suggesting that US share some neurological vulnerability with probands. Sex-comparison studies have indicated that ASD is associated with sex-specific neurological effects. However, ASD girls have been grossly understudied relative to boys and no study to date has implemented diffusion tensor imaging (DTI) in the exclusive examination of girls with ASD or US.

Objectives:

Investigate WM structure in ASD girls in comparison to neurotypical (NT) girls and US sisters.

Methods:

This study consisted of 31 girls: 13 ASD (mean age:8.9yr; IQ:101), 11 NT (mean age:9.3yr; IQ:102), and 7 US (mean age:12yr; IQ:102). Participants underwent diffusion-weighted MRI ($2.5mm^3$; 30 directions at $b=1000s/mm^2$; 5 b=0; runs=3) on a 3T Siemens scanner. Diffusion volumes with excessive motion were removed prior to averaging acquired runs. Averaged scans were pre-processed using FSL, including eddy current correction and estimation of the diffusion tensor, which enables calculation of WM microstructure metrics: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD). Voxel-wise group comparisons in WM microstructure were performed using TBSS which co-registers all diffusion data and generates an average WM skeleton on which statistical comparisons are made. The values for each WM metric were also averaged across the WM skeleton and correlated with parent-reported social responsiveness scale (SRSp) t scores. Age and full-scale IQ were covariates.

Results:

There were widespread regions of the right hemisphere in which MD was significantly elevated in US compared to NT. There were also significant clusters widespread in the left hemisphere where RD was significantly higher in ASD compared to NT (both $p<0.05$; FWE-corrected). No other group comparisons reached significance. SRSp score was strongly correlated with DTI measures averaged across the WM skeleton (FA: $p=0.002$; MD and RD: $p<0.001$; AD: $p=0.009$) in NT girls. SRSp and WM correlations did not reach significance in ASD or US. Voxel-wise correlations within TBSS ($p<0.05$; FWE-corrected) showed that the NT FA and RD relationships with SRSp were widespread bilaterally, whilst the MD-SRSp relationship was localised to the left hemisphere. The AD correlation did not show a significant voxel-wise effect.

Conclusions:

This is the first study to show that both ASD girls and US sisters have WM abnormalities in comparison to NT girls, thus indicating that siblings and probands exhibit structural abnormalities in the brain. In controls, SRSp score, a measure of ASD-like behaviours, was highly related to WM microstructure; this relationship was not observed in the other groups. This suggests that both ASD girls and US

sisters show an atypical relationship between WM microstructure and ASD traits.

## 167 Early Development II

*Organizer:* W. L. Stone *University of Washington*

**167.001** A Multi-Site Study of Prevalence, Incidence, and Age at First Diagnosis for Autism Spectrum Disorders: Findings from the Mental Health Research Network Autism Registry Study. V. Yau*[1], F. L. Lynch[2], J. Madden[3], A. A. Owen-Smith[4], K. J. Coleman[5], S. Bent[6], M. L. Massolo[7], K. A. Pearson[2], P. Crawford[2], M. E. Pomichowski[5], M. Lakoma[3] and L. A. Croen[7], (1)*Kaiser Permanente*, (2)*Kaiser Permanente Northwest*, (3)*Harvard Pilgrim Health Care Institute*, (4)*Kaiser Permanente Georgia*, (5)*Kaiser Permanente Southern California*, (6)*University of California San Francisco*, (7)*Kaiser Permanente Northern California*

Background:

Reported prevalence of autism spectrum disorders (ASDs) in the US has increased from 0.45/1000 children in the 1960s to approximately 11.3/1000 in 2008. Prevalence statistics vary greatly depending on study methodology and demographics of the populations.

Objectives:

The objective of this study was to pool data from several large health systems across the US to investigate trends in ASD prevalence, incidence, and age at first diagnosis from 1997-2010, and to assess variation in trends across demographic factors.

Methods:

Children born between January 1, 1993 and December 31, 2008 and members of one of five health plans in the Mental Health Research Network Autism Registry project were included: Kaiser Permanente (KP) Northern California, KP Northwest, KP Southern California, KP Southeast, and Harvard Pilgrim Health Care. Children with an ASD diagnosis from an ASD specialist or two or more ASD diagnoses from non-specialists recorded in medical records were considered to have ASD. Annual prevalence was based on individuals with any health plan membership in that particular year. Annual cumulative incidence and median age at first diagnosis were calculated for each birth year cohort and included children with 6 or more months of membership in each year of life (with the exception of the first year after birth).

Results:

We identified a total of 24,062 children with ASD among a total pediatric population of 3,938,603 born in the study years. Among children aged 5-9 years in a given year, prevalence of all ASDs increased steadily from 1.5/1000 in 1998 to 12.0/1000 in 2010 with similar increases in Autistic Disorder or AD (1998: 1.0/1000, 2010: 8.5/1,000) and non-AD ASD (1998: 0.5/1000, 2010: 3.4/1000).

Prevalence of all ASDs in children aged 5-9 years in 2010 varied by race/ethnicity (White: 20.1/1000, Black: 15.6/1000, Asian: 17.2/1000, Hispanic: 14.0/1000). Prevalence of ASDs among males aged 5-9 years was higher than among females (2010: males = 23.8/1000, females = 5.5/1000).

Incidence of all ASDs before age 6 increased steadily (1997 Birth Cohort: 4.8/1000, 2005 Birth Cohort: 12.2/1000), as did incidence of AD (1997: 3.7/1000, 2005: 9.0/1000) and non-AD ASD (1997: 1.1/1000, 2005: 3.1/1000). Median age of first diagnosis among children aged 5 or lower fell from 4.77 for children born in 1996 to 3.07 for 2005 births. Median age at first diagnosis for 2005 births did not vary much by race/ethnicity (Blacks: 3.07, Asians: 3.01, Hispanics: 3.10, Whites: 3.02).

Conclusions:

This study provides up-to-date prevalence and incidence information from several large, diverse, and health-insured populations. Prevalence and incidence of ASDs and ASD subtypes increased over the years while median age of diagnosis fell. Differences in results across race/ethnic groups require further exploration.

**167.002** Vocal Coordination during Early Parent-Infant Interactions Predicts Language Outcome in High Risk Infants. J. B. Northrup* and J. M. Iverson, *University of Pittsburgh*

Background:

Like adults, typically developing infants and their mothers adjust the timing of their vocal behavior to coordinate with their conversational partner. This type of coordination begins as early as 4

months of age and is related to developmental outcomes (Beebe et al., 1988; Jaffe et al., 2001).

Due to strong genetic etiology, infant siblings of individuals with autism spectrum disorder (ASD) are at high risk (HR) for being diagnosed not only with ASD, but also with significant language delays (Zwaigenbaum et al., 2005). Studies comparing HR infants to infants without an older sibling with ASD (low risk infants, LR), have revealed early differences in social communication, allocation of attention, and synchrony with an interactive partner (Paul et al., 2011; Droucker et al., 2013; Yirmiya et al., 2006), all of which have implications for vocal coordination.

Objectives:

The aim of this study is to examine the vocal characteristics of mother-infant interactions in a HR sample in order to better understand the development of infants at risk for autism as well as the common occurrence of language delays in this population.

Methods:

Participants include 35 nine-month-old infants (25 HR; 10 Low Risk: LR) videotaped at home during a 5-minute unstructured toy play interaction with their mothers. All mother and infant vocalizations and periods of silence were coded on a moment-by-moment basis, generating the following variables: frequency of vocalizations, average duration and variability of latency to respond (the time between when one person stops speaking and the partner's response), average duration of intrapersonal pause (the time between two vocalizations of the same speaker), and frequency of interruptions (when one speaker speaks during a partner's vocalization).

All HR infants were followed longitudinally to 36 months, and two standardized measures of language (Macarthur Bates Communication Development Inventory and Mullen Scales of Early Learning) were administered at 18, 24, and 36 months. We used these measures to classify infants as language delayed (LD) and to create a continuous measure of language ability in toddlerhood.

Results:

HR mothers had more variable latencies to respond than LR mothers ($p=0.026$). Mothers and infants in LD dyads were more likely to interrupt each other than mothers and infants in ND dyads ($p's<0.05$). LD mothers and infants were also less correlated with one another ($r = -.02$,n.s.) in average duration of latency to respond than ND dyads ($r =0.81$,$p<.001$), and the degree of similarity between mothers and infants on this variable predicted a continuous measure of language development in toddlerhood ($p<.001$). A binary logistic regression predicting Outcome (LD vs. ND) with frequency of infant and mother interruptions and coordination of latency to respond correctly classified 85% of the infants as LD or ND ($X^2=14.63$, $p=0.002$).

Conclusions:

Results indicate that differences in the ability to coordinate vocalizations with those of a partner in an interaction are predictive of later language outcome. Findings will be discussed in terms of early markers of language delay and the potential cascading effects of early delays on development.

**167.003** Reduced Curiosity and Exploration As an Early Warning Sign of ASD. E. C. Bacon*[1], M. Chen[2], L. Schreibman[1], A. C. Stahmer[3], C. Carter[1], E. Courchesne[1] and K. Pierce[1], (1)*University of California, San Diego*, (2)*UCLA*, (3)*University of California San Diego*

**Background:** Researchers and clinicians have sought to diagnose children with ASD at the youngest ages possible, but the slow emergence of symptoms during the first two years of life makes this a challenge. Ideally, novel behavioral markers of ASD would be discovered that are found in both early and late-onset ASD. Exploring the environment is one mechanism that typically developing toddlers use to bootstrap sensor-motor development and joint attention skills. Restricted interests in ASD toddlers may interfere with this important early behavior, and be observable during free play situations.

**Objectives:** Examine behavioral markers associated with both early and late-onset cases of ASD.

**Methods:** 255 participants (mean age = 15 months) were recruited from a large scale longitudinal study examining early development of ASD in toddlers. Participants were evaluated every 6-12 months until age three on several diagnostic

(e.g., ADOS) and experimental measures (e.g., exploration). Four diagnostic comparison groups were included; early-onset ASD (mean age of diagnosis =17.73 months; n=55), late-onset ASD (no ASD diagnosis at initial assessment, mean age of ASD diagnosis= 24.94 months; n=37), language delay (LD, n=55), and typically developing children (TD, n=108).

To measure exploration, toddlers were observed in a room with functional (e.g., ball) and nonfunctional (e.g., piece of string) toys placed in standardized locations (Pierce & Courchesne, 2001). Some toys were inside difficult to open containers and some were on the floor. Videos from the participants' initial evaluation were coded to evaluate exploration including the number of toys and containers explored, amount of time exploring, and movement about the room.

**Results:** Data have been analyzed for 190 participants; ASD early-onset (n=42), ASD late-onset (n=32), LD (n=38), TD (n=78). A MANOVA revealed a significant effect of diagnosis on for both the number of items explored ($F(3, 186)=7.872$, $p<.000$) and the number of containers explored ($F(3,186)=4.656$, $p=.004$). The TD group explored significantly more items (M=12.12) than either the early-onset ASD (M=8.6, $p<.000$) or late-onset ASD groups (M=9.28, $p=.008$). The TD group also explored more containers (M=4.79) than either the early-onset ASD (M=2.83, $p<.010$) or late-onset ASD group (M=2.66, $p<.013$). The LD group also explored more items (M=10.34) and containers (M=3.32) than either ASD group, but these differences were not significant.

**Conclusions:** Children with early-onset ASD and late-onset ASD explored fewer items and containers than TD children. These data suggest exploration is an observable behavioral feature associated with ASD and identifies an easy-to-implement assessment that can capture these features in a young population. Notably, children with late-onset ASD performed similarly to children with early-onset ASD on their initial assessment, prior to their diagnosis of ASD, suggesting late-onset ASD cases may show measureable characteristics associated with ASD before showing enough clear symptoms to receive a diagnosis. Although not significant, both ASD groups also showed reduced exploration in comparison to the LD group. Further research comparing ASD from other developmental delays is needed to identify early behaviors highly specific to ASD. Further analyses of the quality of exploration and play are currently being examined and will be presented.

**167.004** Definition, Measurement, and Validation of Resilience and Canalization in the Early Autism Phenotype. M. Elsabbagh*[1] and .. The BASIS Team[2], (1)*McGill University*, (2)*BASIS*

Background: Autism symptoms in toddlerhood result from early emerging brain function differences observed across multiple systems. These initially subtle differences become compounded and amplified due to atypical interactions within developing brain systems and with the external environment (Elsabbagh and Johnson, 2010). The reasons why this compounding occurs in some infants but not in others, especially in cases of familial risk, remains unknown. While a majority of infants at risk will not develop autism as toddlers, they exhibit highly variable pathways. Some have suggested the preliminary possibility that at least in some cases of familial risk, the infant brain may spontaneously re-organize in order to prevent the onset of disabling symptoms from emerging later on (Elsabbagh, 2012). No study has yet operationalized or validated putative canalization.

Objectives: We previously reported a characteristic brain function response to static faces displaying direct vs. averted gaze in infants at-risk who go on to exhibit typical outcomes in toddlerhood. The control group and infants who later develop autism showed no differentiation between direct and averted gaze. We interpreted this pattern as reflecting recruitment of unique and potentially protective neural mechanisms in this group, i.e., canalization. The objective of the current study is to validate this preliminary possibility by investigating potential associations between these brain function mechanisms and more naturalistic measures of parent-child interaction. If these neural differences indeed reflect protective operations, they should be associated with more optimal individual infant behavior within the context of dyadic interactions.

Methods: Participants were drawn from the British Autism Study of Infant Siblings and included 104 (54 at-risk and 50 control) 7-month-old infants. Approximately 30% of the infants in the at-risk group received an autism diagnosis at 3-years.

Data from two tasks were used for the current study. In the first task, ERPs were recorded while infants viewed images of female faces with static direct vs. averted gaze. The second task was a Parent-child interaction (PCI) assessment, where a 6-min episode of unstructured play was videotaped during which the parent-infant dyad was seated on a floor mat in a room with a small set of toys.

Results: Our findings suggest that P400 response differentiation to direct vs. averted gaze, a pattern unique to the infants at-risk who exhibit typical outcomes in toddlerhood, was associated with parent-child interactions. Specifically, a larger P400 response difference is associated with enhanced infant positive affect (r= .551 p <.001) and dyadic mutuality (r= .553; p=.009). The same associations were not observed in the control group nor in infants at-risk who went on to develop ASD, reflecting recruitment of unique neural mechanisms early in life for a subset of infants who 'canalize' the impact of risk.

Conclusions: There is enormous value in characterizing and understanding factors promoting brain reorganization; such cases potentially inform how early environments can be modified to prevent disabling consequences from emerging. Our findings suggest that patterns of canalization are measurable early on and associated with more optimal behavior of the infant within their familial environments.

**167.005** Analysis of Crying during the Separation Phase of the Strange Situation Procedure in Infant Siblings at High Risk for ASD.

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Background: To better understand social communication during early development, a growing literature is assessing the vocal production of children with Autism Spectrum Disorders (ASD). Previous studies have provided preliminary evidence that disruptions in cry acoustics may be part of an atypical vocal signature of autism early in life. In the current research we investigate the acoustic characteristics of cries elicited in a standardized social interaction context, the Strange Situation Procedure (SSP). The SSP is a gold-standard measure of infant attachment security that consists of a series of separations and reunions with the caregiver designed to activate the infant's attachment behavioral system. Infants often become distressed during separations from the caregiver, and the SSP has been used to assess infant affect and emotional reactivity. The SSP is a standardized yet naturalistic way to study distress reactions both in typical populations and in at-risk populations such as toddlers at high risk for ASD.

Objectives: Test whether the acoustic signature of the cries of HR toddlers differ from those of LR toddlers during the standardized separation from the parent during the SSP.

Methods: We examined the acoustic characteristics of cries extracted from the separation phase of the strange situation procedure in a sample of toddler of younger siblings of a child with autism spectrum disorder-autism spectrum disorders (ASD) (high risk, HR) and a low risk (LR) group. Cry samples derived from vocal recordings of 15-month-old HR (n = 13) and LR infants (n = 14) were subjected to acoustic analyses.

Results: HR toddlers, compared to those with LR, produced cries that were shorter (HR: $M$ = 22.1, $SD$ = 22.7; LR: $M$ = 45.6, $SD$ = 27.9; $F$ = 7.9 $p$ < .05) and had a higher fundamental frequency (F0) (HR: $M$ = 370.1, $SD$ = 30.5; LR: $M$ = 330.0, $SD$ = 26.8; $F$ = 16.8 $p$ < .05). Three HR toddlers later classified with an ASD at 36 months (autistic disorder in all cases) produced cries that had among the highest F0 and shortest durations.

Conclusions: Using a standardized social elicitor, we found that 15-month-olds at high risk for ASD had shorter cry utterances that had higher fundamental frequencies than low-risk toddlers. Strikingly, those HR toddlers later diagnosed with ASD had amongst the most extreme values in the sample. This concordance between the risk group and diagnosed children suggest that disturbed cry patterns, although not a core communication deficit in children with ASD, may provide an early marker of risk for later autism. Understanding the stability of these cry characteristics and their potential impact on the parent–child relationship will require continued longitudinal follow-up of high risk siblings in their family context beyond the age of first diagnosis.

**167.006** The Integration of Vocalizations and Smiles within Joint Attention Acts in Infants at Risk for Autism Spectrum Disorder. L. V. Ibanez*[1], S. R. Edmunds[1], D. Gangi[2], T. P. Nguyen[1], Z. E. Warren[3], D. S. Messinger[2] and W. L. Stone[1], (1)*University of Washington*, (2)*University of Miami*, (3)*Vanderbilt University*

Background:

Although it is clear that impaired levels of social-communicative behaviors are hallmark deficits of ASD, children with ASD are not devoid of such abilities. Examining the manner in which different communicative behaviors are integrated within a particular social communicative bid, in addition to their frequency of occurrence, may be necessary for detecting subtle differences in the early behavior of infants who are *developing* ASD relative to those who are not. To our knowledge, no study to date has examined how the integration of initiating joint attention bids (IJA) with *both* positive affect and vocalizations develops in infant siblings of children with ASD (high-risk infants) relative to low-risk infants.

Objectives:

The objectives of this study are to: 1) examine the morphology of joint attention bids in 12 month old infants, 2) identify differences between groups of high- and low-risk infants, and 3) examine the extent to which the integration of vocalizations and/or smiles predicts ASD symptomatology at 24 months.

Methods:

High-risk infants ($n$=32) and low-risk infants ($n$=19) were examined at 12 and 24 months as part of a larger longitudinal multisite study. At 12 months, IJA bids were coded during the Early Social Communication Scales. Vocalizations were coded if they occurred within 2 seconds of the onset or offset of an IJA bid and smiles were coded if they overlapped with the IJA bid. Four categories of IJA bids were derived: isolated bids without smiles or vocalizations; bids that integrated vocalizations only; bids that integrated smiles only; and bids that integrated *both*vocalizations and smiles. Each category was represented as a percent of total IJA bids. At 24 months, the ADOS severity score (Gotham et al., 2009) was calculated for use as a continuous measure of ASD symptomatology.

Results:

Independent $t$-tests revealed no significant mean differences between high-risk and low-risk infants on total IJA or any of the four categories of IJA bids, $p$s=.54-.92. Total IJA bids did not predict ASD symptomatology at 24 months for high-risk infants or low-risk infants. However, among high-risk infants only, the percent of IJA bids that integrated *both* smiles and vocalizations was negatively associated with later ASD symptomatology, $r(27)=-.40$, $p=.03$, and the percent of IJA bids *without* vocalizations or smiles was positively associated with later ASD symptomatology, $r(27)= .55$, $p=.01$. There were no significant associations between other categories of IJA bids and later ASD symptomatology among high-risk or low-risk infants, $r$s=.05-.32.

Conclusions:

Characterizing the morphology of IJA bids by examining the presence of vocalizations and/or smiles may be helpful in identifying the later emergence of ASD symptomatology, even when overall levels of IJA do not. For example, failing to integrate smiles or vocalizations with IJA bids may signal less enjoyment and motivation to engage with a social partner, representing suboptimal social interactions with later implications for ASD symptomatology. Additional coding is ongoing and developmental changes between 12-18 months will be examined for each IJA category.

**167.007** Early Trajectories of Growth in Initiating Joint Attention Are Associated with ASD Severity at 36 Months. D. Gangi*[1], L. Ibanez[2], W. L. Stone[2] and D. S. Messinger[1], (1)*University of Miami*, (2)*University of Washington*

Background: Infant-initiated joint attention (IJA) is the capacity to use gaze and gesture to share awareness of experiences or events with a social partner. This ability typically emerges during the first year of life, and is an important precursor of later social competence. IJA is impaired in children with Autism Spectrum Disorder (ASD) and may presage ASD symptomatology in their later-born siblings. For example, Ibañez, Grantz, and Messinger (2012) reported that levels of IJA at 8 months in high-risk siblings (those with an older sibling diagnosed with ASD) predicted later ASD symptom severity at 30 months, but did not have a measure of symptom severity at 36 months.

Objectives: To determine whether IJA in the first year of life predicts ASD symptom severity at 36 months in an independent sample of high-risk siblings.

Methods: High-risk siblings ($n$= 42) were administered the Early Social Communication Scales (ESCS; Mundy et al., 2003) at 6 and 9 months of age. ESCS assessments were coded for episodes of IJA (e.g., gaze from active toy to examiner), and the total number of IJA episodes was divided by the length of the ESCS to create rates per minute. The Autism Diagnostic Observation Schedule (ADOS) was administered at 36 months. Calibrated ASD severity scores were calculated for each child to provide a continuous measure of ASD symptomatology (Gotham, Pickles, & Lord, 2009). Clinical best estimate diagnosis was given at 36 months by a licensed clinical psychologist.

Results: Hierarchical linear modeling was used to examine initial levels and growth in IJA from 6 to 9 months in high-risk siblings and to examine associations with ASD diagnosis and severity. Growth in IJA was significant between 6 and 9 months, $\beta_{10} = 0.96$, $t(28) = 3.69$, $p = .001$. Growth did not differ by diagnostic outcome (ASD [n=8] or no ASD [n=23]), $\beta_{11} = -0.76$, $t(28) = -2.01$, $p = .054$. By contrast, growth in IJA from 6 to 9 months was associated with ASD severity at 36 months, with lower rates of growth associated with higher ASD severity scores, $\beta_{11} = -0.14$, $t(28) = -2.84$, $p = .009$. Correlations, which provide an effect size, confirmed that estimates of slope, $r(30) = -.47$, $p = .01$, as well as 9 month levels of IJA, $r(28) = -.43$, $p=.02$, were associated with ASD severity.

Conclusions: The rate of high-risk siblings' growth in IJA from 6 to 9 months was negatively associated with later ASD symptomatology at 36 months. Early upward trajectories of IJA growth—in the period when infants develop referential communication—appear to be relatively sensitive predictors of symptom level—although not diagnosis—in high-risk siblings. As in Ibañez et al., levels of IJA before 12 months were predictive of three year ASD symptomatology. In both studies, IJA was elicited in the ESCS, a routine, standardized, semi-structured task with an examiner. The current study shows in a second, independent sample that high-risk infants' early ability to share an experience with a social partner is associated with later ASD symptomatology.

**167.008** Developmental Trajectories of Respiratory Sinus Arrhythmia in Children with Autism from Birth to Early Childhood.

S. J. Sheinkopf*[1], T. P. Levine[1], B. Abar[1], E. Conradt[1], L. L. LaGasse[1], R. Seifer[2], S. Shankaran[3], H. Bada-Ellzey[4], C. Bauer[5], T. M. Whitaker[6], J. A. Hammond[7] and B. M. Lester[1], (1)*Women & Infants Hospital*, (2)*Warren Alpert Medical School of Brown University*, (3)*Wayne State University*, (4)*University of Kentucky*, (5)*Miller School of Medicine, University of Miami*, (6)*The University of Tennessee Health Science Center*, (7)*RTI International*

**Background:** Physiologic systems regulating arousal and attention are thought to be affected in autism and appear to be related to functioning and deveopmental outcomes in this population. Respiratory sinus arrhythmia (RSA), a measure of heart rate variability and an index of physiological regulation, has been reported to be diminished in autism. However, the development of RSA and related regulatory systems in infants later diagnosed with autism has not been studied.

**Objectives:** To examine physiological regulation in infants later diagnosed with autism by modeling the longitudinal trajectory of heart rate (HR) and RSA in a sample of infants observed from birth and later diagnosed with autism.

**Methods:** Twelve (12) children with autism were identified from the Maternal Lifestyle Study (n = 1388), a longitudinal study of high-risk infants. Autism diagnoses were confirmed by clinician best estimate plus above-threshold scores on the Autism Diagnostic Observation Schedule. A case control design was utilized to select a comparison sample (n = 106) matched on prenatal risk factors and birth weight. Electrocardiogram (ECG) recordings were collected during standardized observations at 1, 12, 18, 24, 36, 48, 60, and 72 months of age. ECG post-processing incorporated automated artifact detection and correction routines. RSA was calculated from the resulting "cleaned" time series data using Porges' method. Latent growth curve analyses were used to model the developmental course of HR and RSA in the two groups. All models were performed in Mplus 6.0 using a full information maximum likelihood estimator to account for missing data over time. Unconditional and conditional latent growth curve (LGC) models were performed to demonstrate the overall HR and RSA trajectories as well as the effect of autism diagnosis on growth trajectories.

**Results:** Unconditional LGC models demonstrated an expected age-related decrease in HR and increase in RSA over time. Conditional LGC models (including autism diagnosis) did not show an effect of diagnosis on the decrease of HR over time ($p$ = 0.23). With regard to RSA, children with autism demonstrated a smaller linear increase over time than comparison children ($p$ < 0.01). There was also a significant effect of diagnosis on the quadratic trend for RSA ($p$ < 0.01). Children with autism demonstrated a stronger flattening/downturn in RSA at later ages than comparison children. There was no effect of diagnosis on initial level of RSA ($p$= 0.30).

**Conclusions:** These results suggest that differences in physiological regulation may develop with age in autism. Developmental change in RSA was slower in infants later diagnosed with autism. This slowed RSA growth in autism was most evident after 18 months of age, at a time when behavioral symptoms become prominent. This is consistent with the view that RSA is a marker of functional status in autism and raises the hypothesis that differences in RSA emerge developmentally. Larger studies are needed to determine if differences are present earlier in infancy. Longitudinal studies of developmental trajectories such as this will have implications for the timing and targets of treatment in infants at risk for autism.

## 168 Diagnostic and Behavioral Assessment and Measurement

*Organizer:* S. Ozonoff *University of California Davis Medical Center*

**168.001** Video-Referenced Ratings of Reciprocal Social Behavior in Toddlers: A Twin Study. N. Marrus*, Y. Zhang, E. L. Mortenson, K. Holzhauer, S. Sant, V. Hariprasad, A. Glowinski and J. N. Constantino, *Washington University School of Medicine*

Background: Reciprocal social behavior (RSB) is a developmental prerequisite for social competency, and severe deficits in RSB constitute a core feature of autism spectrum disorder (ASD). Although several clinical measures screen for ASD-related impairment in young children, feasibly *quantifying* RSB across its full range of variation in early childhood, when ASD first arises, remains an important priority, especially for large-scale developmental studies and for measuring incremental response to early intervention. Since caregivers of preverbal children might have difficulty differentiating nuances of social communication, we developed a video-referenced system for rating early RSB (vr-RSB) in which a rater first views a 3-minute video clip depicting highly competent social behavior in a toddler, and then compares the subject he/she is rating with the child in the video clip, who serves as a scoring anchor for 13 quantitative video-referenced items on the scale.

Objectives: To examine the psychometric properties of vr-RSB measurements at ages 18-24 months, their relationship to scores on screeners for ASD and language delay, and twin-twin correlations as a function of zygosity.

Methods: Parents of 162 epidemiologically-ascertained twins (MZ=20 pairs, DZ=61 pairs) rated their children using the vr-RSB and two developmental screeners, the Modified Checklist for Autism in Toddlers (M-CHAT), and the MacArthur Communicative Development Inventory Short Form (MCDI-s). At the time of this writing, test-retest data for the vr-RSB were available for 37 subjects.

Results: In contrast to the screeners, scores on the vr-RSB were fully continuously distributed, with excellent 3-month test-retest reliability (ICC=0.76, p=0.000). Monozygotic twins displayed markedly greater trait concordance than dizygotic twins, (MZ ICC=0.886, p=0.000, DZ ICC =0.197, p=0.063), suggesting substantial heritability of this measurement. Scores on the vr-RSB distinguished subjects with passing versus failing scores on the M-CHAT (t=-5.293, df=19.882, p=.000), and were inversely correlated with number of words produced on the MCDI-s (r=-0.272, p=0.001), showing an association between decreased deficits in RSB and increased expressive vocabulary.

Conclusions: vr-RSB scores in toddlers exhibit a continuous, quantitative distribution, as has been observed for RSB throughout the lifespan. Rapid video-referenced ratings of RSB appear highly heritable, similar to ASD, and can distinguish toddlers at elevated risk of ASD. The correlation of vr-RSB scores and language scores, demonstrated here in a normative population, suggests that further investigation of the relationship between the early capacity for RSB and language function is relevant for understanding behavioral development in both

children with ASD and typically developing children. These results support the potential utility of video-referenced ratings for quantifying the capacity for early RSB in public health settings and monitoring incremental response to early intervention. These findings also have implications not only for promoting earlier identification of ASD, but also for elucidating the genetic-environmental structure of early RSB in typical and atypical development.

**168.002** A Critical Review of Outcome Measures Used to Evaluate the Effectiveness of Comprehensive, Community-Based Treatments for Preschoolers with ASD. M. Stolte*[1] and S. Hodgetts[2], (1)*Centre for Autism Services Alberta*, (2)*University of Alberta*

**Background**: Central to the effective evaluation of program outcomes are the tools chosen to measure those outcomes. Comprehensive treatment programs for preschoolers with ASD vary widely in their treatment targets, and as such, outcome measures used across studies vary considerably. This variability has implications for clinical uptake of this data and for choosing the "optimal" outcome measures for research. Additionally, tool usage modifications, justification, and adherence to clinical assessment and reporting requirements impact test score confidence and generalizability of the results. The overall aim of this review was to summarize and critically evaluate how standardized tests are used as outcome measures for comprehensive community-based interventions for preschool-aged children with ASD.

**Objectives**:

1. Summarize the most frequently targeted treatment outcomes;
2. Summarize the dominant tools being used to measure these treatment outcomes;
3. Critically evaluate the use of these tools in terms of their intended usage, construct representation, and reporting requirements.

**Methods**: A variety of medical, educational and allied health databases were searched for studies published between 2004 and 2012 using various combinations of the keywords "community", "intervention", "treatment", "outcome", "preschool" and "autism". After reviewing 200 studies, a total of 24 met the inclusion criteria. Outcome instruments were (1) identified, (2) categorized (cognitive, adaptive, language/communication, behaviour/autism symptomology), and (3) compared to criteria identified in the *Standards for Educational and Psychological Testing (The Standards*; AREA, APA, & NCME, 1999), a best practice framework created to guide the development, validation, administration, reporting, and appropriate use of educational and psychological tests, including those used with with children of ASD.

**Results**: A total of 32 different outcome measures were identified across the 24 studies. Cognitive (83%) and adaptive behaviour (96% of studies) were the primary tools of outcome-based measurement for comprehensive autism treatment. Specifically, the Vineland Adaptive Behavior Scales (VABS) was the most frequently reported outcome measure, used in 92% of the studies reviewed, raising a possibility of systemic measurement bias. Behavioral and autism-specific (67% of studies), and language (42% of studies) tools were under-represented, despite these being central constructs of autism. The following *Standards* criteria were relatively well met: including the use of multiple outcome tools (83%), clear sample description (100%), and using tools that represented each of the three constructs associated with ASD (75%). However, concerns included an over-reliance on a single adaptive measure, substitution of different pre and post cognitive measures despite different theoretical constructs (58% of studies), under-reporting of technical information and justification for tests selected (38%), lack of reported assessor blindness to treatment condition (only 13%), and an under-reporting of administration procedures (8%) and test modifications (0% of studies).

**Conclusions**: Cognitive and adaptive measures continue to be primary outcome tools for ASD treatment, despite a lack of clear fit to core ASD constructs. Substitution of different cognitive tools and adaptive measurement bias is also a concern. However, most of the reviewed studies met much of the criteria outlined in the *Standards*, with some reporting exceptions on test modifications and assessor blindness. Clinical and research implications will be discussed.

**168.003** DSM-5 Autism Spectrum Disorder: In Search of Essential Behaviours for Diagnosis. S. R. Leekam[1], S. J. Carrington*[1],

R. G. Kent[1], J. Gould[2], L. Wing[2], J. P. W. Maljaars[3], I. Noens[3], I. A. van Berckelaer-Onnes[4] and A. S. Le-Couteur[5], (1)*Cardiff University*, (2)*National Autistic Society*, (3)*KU Leuven*, (4)*Universiteit Leiden*, (5)*Newcastle University*

Background: Despite initial concerns about the sensitivity of the proposed diagnostic criteria for DSM-5 Autism Spectrum Disorder (ASD; e.g. Gibbs et al., 2012; McPartland et al., 2012), evidence is growing that the DSM-5 criteria provides an inclusive description with both good sensitivity and specificity (e.g. Frazier et al., 2012; Kent, Carrington et al., 2013). The capacity of the criteria to provide high levels of sensitivity and specificity comparable with DSM-IV-TR however relies on careful measurement to ensure that appropriate items from diagnostic instruments map onto the new DSM-5 descriptions.

Objectives: To use an existing DSM-5 diagnostic algorithm (Kent, Carrington et .al., 2013) to identify a set of 'essential' behaviors sufficient to make a reliable and accurate diagnosis of DSM-5 Autism Spectrum Disorder (ASD) across age and ability level.

Methods: Specific behaviors were identified and tested from the recently published DSM-5 algorithm for the Diagnostic Interview for Social and Communication Disorders (DISCO). Analyses were run on existing DISCO datasets, with a total participant sample size of 335. Three studies provided step-by-step development towards identification of a minimum set of items. Study 1 identified the most highly discriminating items ($p<.0001$). Study 2 used a lower selection threshold than in Study 1 ($p<.05$) to facilitate better representation of the full DSM-5 ASD profile. Study 3 included additional items previously reported as significantly more frequent in individuals with higher ability. The discriminant validity of all three item sets was tested using Receiver Operating Characteristic curves. Finally, sensitivity across age and ability was investigated in a subset of individuals with ASD ($n=190$).

Results: Study 1 identified an item set (14 items) with good discriminant validity, but which predominantly measured social-communication behaviors (11/14). The Study 2 item set (48 items) better represented the DSM-5 ASD and had good discriminant validity, but the item set lacked sensitivity for individuals with higher ability. The final Study 3 adjusted item set (54 items) improved sensitivity for individuals with higher ability and performance and was comparable to the published DISCO DSM-5 algorithm.

Conclusions: This work represents a first attempt to derive a reduced set of behaviors for DSM-5 directly from an existing standardized ASD developmental history interview. Further work involving existing ASD diagnostic tools with community-based and well characterized research samples will be required to replicate these findings and exploit their potential to contribute to a more efficient and focused ASD diagnostic process.

**168.004** Evidence of Robust Tools for the Evaluation of Outcomes in Young Children with ASD.

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Background:

One problem for researchers evaluating early intervention, and for providers of services for young children with autism spectrum disorder (ASD), is the multitude of outcomes assessed and measurement tools used to collect evidence about children's progress. Relevant outcomes include improvement in core ASD impairments such as communication, social awareness, sensory sensitivities and repetitiveness; skills such as social functioning, behaviour and play; participation outcomes such as social inclusion; and parent and family impact. Each type of outcome has multiple tools which might be used; however, systematic appraisal of the measurement properties of these tools, and qualities such as ease of use and acceptability to children and parents is lacking. This systematic review was commissioned by the UK National Institute for Health Research.

Objectives:

To examine the measurement properties of tools used to measure progress and outcomes in children with ASD up to age 6 years. Further, to identify outcome areas in which evidence is lacking.

Methods:

The MeASURe research collaboration includes ASD experts and review methodologists. We undertook:

A: systematic review of tools used in ASD early intervention and longitudinal studies from 1992 to 2013.

B: systematic review of papers addressing the measurement properties of identified tools in children with ASD, using the COSMIN checklist (Consensus-based Standards for the selection of health Measurement Instruments).

C: synthesis of evidence and gaps, and consultation about recommendations with stakeholders including parents, young people with ASD, clinicians, and researchers.

Results:

The conceptual framework for the review was drawn from the International Classification of Functioning, Disability and Health, including the domains of 'impairments', 'activity limitations', 'participation restrictions', and family measures. In A, 10,261 papers were sifted, 3088 by full text, and data extracted from 181. In total 129 tools were identified, excluding observational coding, those developed for a particular study and those not in English. In B, 2,793 papers were sifted and data extracted from 128 concerning 52 (40%) tools. For the remainder, no measurement properties study including children with ASD was identified.

The review will be completed in March 2014. Evidence for the measurement properties of tools will be presented, along with information about their accessibility and strengths/weaknesses in use. The obvious gaps in available assessment tools include measurement of wellbeing and participation outcomes for children, and family quality of life.

Conclusions:

This is the first review of the quality and appropriateness of tools to monitor young children's progress and outcomes which has collated systematically the available evidence on measurement properties of the tools. With input from parents and other stakeholders, we will present consensus recommendations about a set of tools to be used in future by researchers and service providers.

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**168.005** How Can We Robustly Measure Sensory Reactivity; A New DSM-5 Criterion for Autism Spectrum Disorder. T. Tavassoli*[1], K. Bellesheim[2], J. J. Servinskas[3], D. Grodberg[3], A. Kolevzon[3] and J. D. Buxbaum[3], (1)*Mount Sinai School of Medicine, Seaver Autism Center*, (2)*University of Missouri*, (3)*Icahn School of Medicine at Mount Sinai*

Background:

Sensory reactivity abnormalities are a new criterion for Autism Spectrum Disorder (ASD) in the latest Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Yet a consensus on how we can reliably measure sensory reactivity in clinical and research settings is missing.

Objectives:

The current study set out to compare existing methods in order to identify robust measures of sensory reactivity.

Methods:

To assess sensory reactivity in children with ASD (n=35) and without (n=27), three measures were employed: two sensory questionnaires (Short Sensory Profile and Sensory Processing Scale Inventory) and one sensory observation (Sensory Processing Scale Assessment). ADOS and ADI-R were used for ASD diagnosis.

Results:

Children with ASD showed more sensory reactivity abnormalities on all three sensory measures compared to typically developing children. Sensory reactivity abnormalities were present in 47% of cases on the two questionnaires and in 64% of cases on the observation. The three sensory reactivity measures overlap in identifying abnormalities, and they also correlate moderately with one another. Inter-rater reliability ranked from .52 to .74, with the highest agreement between both parent-reports.

Conclusions:

We confirmed that a significant amount of children with ASD (47-64%) have sensory reactivity issues using three sensory measures, two parent-reports and one observation. The three measures overlap between 52% and 74% of the time in classifying individuals as having sensory reactivity difficulties, which is important for clinical and research settings wanting to examine the new DSM-5 criteria of sensory reactivity. Given that the overlap is only moderate the three different sensory measures seem to measure different aspects of sensory reactivity. Therefore we recommend using at least one sensory parent report and in addition a sensory observation.

**168.006** Diagnostic Testing Practices for Autism Spectrum Disorder in Four US Populations. C. E. Rice*[1], L. A. Carpenter[2], L. D. Wiggins[3], N. C. Hobson[4], L. C. Lee[5], J. Baio[3], S. Pettygrove[6], L. B. King[2], C. C. Bradley[2] and M. J. J. Morrier[7], (1)*National Center on Birth Defects and Developmental Disabilities*, (2)*Medical University of South Carolina*, (3)*Centers for Disease Control and Prevention*, (4)*Research Triangle Institute*, (5)*Johns Hopkins Bloomberg School of Public Health*, (6)*University of Arizona - Tucson*, (7)*Emory University School of Medicine*

**Background:** The use of standardized tools is a recommended professional practice when considering an autism spectrum disorder (ASD), although little research has been done to characterize the use of these tools in community population samples.

**Objectives:** To characterize ASD test use in developmental evaluations of children with ASD.

**Methods:** The Autism and Developmental Disabilities Monitoring (ADDM) Network monitors prevalence and describes characteristics of children with ASD in multiple areas of the United States. Descriptive statistics were used to describe the frequency and types of ASD tests documented in developmental evaluation records and type of community professionals who administered the tests. Chi-square analyses were used to assess differences in ASD test use by surveillance site (i.e., AZ, GA, MD, and SC), child sex, child race/ethnicity, and record type (i.e., education or health).

**Results:** 1,708 eight-year-old children (N=1,438 males and N=270 females) met ADDM *DSM-IV-TR* criteria for an ASD in the 2008 surveillance year after review of evaluation records through age 8 from multiple health and education sources. Of these children, 76.2% had at least one ASD test documented in evaluation records with an average of 3.7 ASD tests per child. Evaluations with ASD tests were administered between 9 and 107 months of age with a median of 70 months. Of all the ASD tests documented, the Childhood Autism Rating Scale was the most commonly used (CARS; 30.4%), followed by the Gilliam Autism Rating Scale (GARS; 26.6%), Autism Diagnostic Observation Schedule (ADOS; 9.7%), Gilliam Asperger Disorder Scale (GADS; 9.4%), Asperger Syndrome Diagnostic Scale (ASDS; 7.0%), and the Autism Diagnostic Interview-Revised (ADI-R; 2.0%). Other ASD tests (e.g., Autism Behavior Checklist) accounted for 14%. ASD tests were most commonly administered by PhD/PsyD/MA psychologists (45.7%); followed by EDD/EDS psychologists (24.8%); developmental pediatricians (14.2%); educators (3.1%); other types of MDs (e.g., neurologists, psychiatrists) (3.0%); speech language pathologists or occupational therapists (2.4%); social workers or licensed counselors (0.4%); and other or unknown professional types (6.4%). Some surveillance sites documented ASD test use more than others ($\chi^2$=55.85, p<0.001), with the greatest proportions of documented testing in SC (86.0%) and the least in MD (68.2%). ASD tests were more frequently administered to boys diagnosed with ASD (77.1%) compared to girls (71.1%) (p<0.05). There were also group differences race and ethnicity of the proportion of children evaluated by an ASD test (p<0.001): Asian or Pacific Islanders (81.6%); black, non-Hispanics (80.0%); white non-Hispanics (75.7%); and Hispanic children (65.0%). ASD tests were more frequently administered in education settings (61.2%) than health settings (38.8%) (p<0.001).

**Conclusions:** While three-quarters of children identified with ASD were evaluated using an ASD test, very few were administered "gold-standard" tools (the ADOS and ADI-R) in in community health and education settings. Testing practices varied by site. ASD tests were administered more frequently to boys than girls, and least frequently to Hispanic children. ASD tests were also administered more frequently in education settings, and by psychologists. These results highlight the need for continued education on the

importance and use of standardized tools for all children evaluated for an ASD.

**168.007** Observation-Centered Approaches to ASD Assessment in Tanzania. A. L. Johnson*[1], E. H. Zimak[2], E. M. Morrow[2] and S. J. Sheinkopf[2], (1)*Alpert Medical School of Brown University*, (2)*Brown University*

Background: In many lower- and middle-income countries, including several African nations, there is a paucity of mental health assessment services for Autism Spectrum Disorders (ASD). Although efforts are being made to increase the availability of culturally appropriate, ASD specific diagnostic tools, at present it is necessary to promote cross-cultural assessment with available resources to ensure globally that individuals with ASD are identified and receiving treatment.

Objectives: An observation-based assessment protocol modeled after best-practice guidelines was adapted for use in Tanzania, a region primarily without diagnostic services. The current study examined behavioral, social and adaptive differences between a group of Tanzanian children diagnosed with ASD and a comparison group of children without ASD, suspected of global delays. Based on our study, guidelines are provided for conducting cross-cultural assessments in the context of limited validated resources.

Methods: We describe the utility of a flexible, behavioral observation instrument, the Childhood Autism Rating Scales, Second Edition (CARS2), to gather diagnostic information in a culturally sensitive manner. In addition, our battery included a measure of adaptive functioning normed for use in Africa, an adapted intake interview, and a non-verbal assessment of cognitive functioning. This approach enabled us to rate DSM criteria in a culturally sensitive manner and to provide differential diagnostic evaluations for 41 children in Tanzania aged 2 to 21 years.

Results: We observed that the ASD group was characterized by significantly higher scores on the CARS2, $t = 4.41$, $p = .001$, and demonstrated significantly more DSM symptoms, $t = 6.92$, $p < .001$, than a general delay comparison group.

Conclusions: Recommendations are provided for making cultural adaptations to current assessment instruments so that ASD differential diagnostic evaluations can be implemented in countries without validated diagnostic instruments, such as Tanzania. This type of assessment battery enables expedited diagnostic services to be provided to individuals in low- and middle-income countries.

**168.008** The CROSS Cultural Examination of a Brief Autism Diagnostic Interview (ADI-R) in KOREA and the United States. L. Daley*[1], C. Keys[2], D. Henry[3], Y. S. Kim[4] and B. Leventhal[5], (1)*DePaul University*, (2)*DePaul Univeristy*, (3)*University of Illinois at Chicago*, (4)*Yale Univeristy*, (5)*University of New York*

**Title:**The Development and Cross Cultural Examination of the Korean Brief Autism Diagnostics Interview (KBADI) and the ADI-R Algorithms in Korea.

**Background:** As countries and cultures around the world become more aware and concerned about autism spectrum disorders, there is a need to develop measures that are grounded in those cultures. The Autism Diagnostic Interview (ADI-R) is an accepted standard method for providing a diagnosis of autism spectrum disorder. The ADI-R has been translated into over thirty languages around the world. At times, clinicians have found it challenging to administer the full ADI-R. This study aims to develop a brief Korean ADI-R that can give more insight into the role of culture and how it can be more grounded in Korean culture.

**Objectives:** To development of the Korean Brief Autism Diagnostic Interview (KBADI) measure for use in the Korean culture. To predict the diagnosis of autism spectrum disorder in Korean children as accuracy with the KBADI as with the Korean-translated ADI-R algorithm for two groups of Korean children: children under the age of ten with fluent language and children ten years of age and older with fluent language.

**Methods:** The total number of participants included 286 school-aged Korean children. This sample of children was part of a larger epidemiological study of autism in South Korea. The Korean-translated Autism Diagnostic Interview (ADI-R) was administered as part of a full diagnostic assessment.

**Results:** A single-parameter item response (IRT) model (Rasch, 1960) was used to select items for the Korean Brief Autism Diagnostic Interview (KBADI) from the full Korean-translated ADI-R. The KBADI is a 23-item measure grounded in Korean culture to provide a diagnosis of autism spectrum disorder. The KBADI measure is

consistent with the criteria of autism; items include deficits in social development, communication, and repetitive/stereotyped behaviors and interests. Correlation analyses revealed that the KBADI and Korean-translated ADI-R algorithms for both groups were strongly correlated. The ROC curve statistics indicated that the Korean Brief Autism Diagnostic Interview (KBADI) can predict the diagnosis of autism spectrum disorders with accuracy comparable to that of the Korean-translated Autism Diagnostic Interview-Revised (ADI-R) diagnostic algorithms for two age groups.

**Conclusions:** This study was successful in creating the KBADI. The KBADI is only 23 items and uses one version from age 7 – 12 and is as accurate as the ADI-R algorithm with this sample. The development of this measure recognized the core characteristics of autism while also accommodating to cultural influences in South Korea.

## 169 Longitudinal Studies and Trajectories: Social, Communication and Repetitive Behaviors

*Organizer:* S. L. Bishop *Center for Autism and the Developing Brain, Weill Cornell Medical College*

**169.001** Walking Onset Predicts Rate of Language Growth in Children with Autism Spectrum Disorder. R. Bedford*[1], A. Pickles[1] and C. Lord[2], (1)*King's College London*, (2)*Weill Cornell Medical College*

**Background:** Motor milestones such as the onset of walking are important developmental markers, not only for later motor skills but also for more widespread social-cognitive development. Early impairments in gross motor skills, including delayed walking onset, atypical gait and postural stability, have been shown in children with autism spectrum disorder (ASD) and it is possible that such difficulties have knock on consequences for language development.

**Objectives:** The aim of the current study was to test whether parent-reported onset of walking predicted the subsequent rate of expressive and receptive language development from 2 – 9 years in a large cohort of children with ASD controlling for non-verbal IQ and autism symptom severity.

**Methods:** We ran growth curve models for expressive and receptive language from the Vineland Adaptive Behavior Scales measured at 2, 3, 5 and 9 years in 209 autistic children. Walking onset (as reported in the Autism Diagnostic Interview-Revised; ADI-R) was included as a predictor of the slope of language development with non-verbal IQ (visual reception; VR, subscale of the Mullen Scales of Early Learning) and autism symptom severity (ADI-R total item score) as covariates. A high proportion of the children showed floor effects of the VR T-score. To characterize the variability in scores at this low end of the scale we also regressed the log of VR-T scores on the log of VR Age Equivalent scores and age at visit 2 and imputed these predicted values.

**Results:** Parent reported age of walking onset significantly predicted the subsequent rate of both receptive (ß = -0.09, S.E. = 0.04, $p$ = 0.03) and expressive (ß = -0.1, S.E. = 0.04, $p$ = 0.03) language development after controlling for VR T-score and severity of ASD symptoms. When the more stringent statistical model accounting for floor effects in VR T-scores was applied these relationships became non-significant (receptive: ß = -0.06, S.E. = 0.04, $p$ = 0.16; expressive: ß = -0.06, S.E. = 0.04, $p$= 0.14), although the trends remained in the same direction. For both receptive and expressive language, scores were similar across early and late walkers when children were young but differed in the oldest children, with lower language scores in the late walkers.

**Conclusions:** As in typical development, results indicate that walking onset is related to subsequent receptive and expressive language development in ASD. Onset of walking appears to influence the rate of language learning, rather than causing an initial boost in language which then persists over time. This suggests that motor delays in young children with ASD can have a longitudinal cross-domain influence, potentially contributing, in part, to the linguistic difficulties which characterise ASD. Various mechanisms have been proposed to underlie this relationship in typical development, including increased joint attention episodes, having hands free to point and gesture, and cerebellar development. Future work is required in children with autism to understand the likely bidirectional interactions between motor and language pathways across development and to elucidate the underlying mechanisms.

**169.002** Early Expressive and Receptive Language Trajectories in High-Risk Infant Siblings of Children with Autism Spectrum Disorder (ASD). J. Longard*[1], S. E. Bryson[2], J. A. Brian[3], L. Zwaigenbaum[4], C. L. Moore[1], E. K. Duku[5], C. Roncadin[6], W.

Roberts[7], I. M. Smith[8], N. Garon[9] and P. Szatmari[7], (1)*Dalhousie University*, (2)*Dalhousie/IWK Health Centre*, (3)*Holland Bloorview Kids Rehab/ University of Toronto*, (4)*University of Alberta*, (5)*Offord Centre for Child Studies & McMaster University*, (6)*Peel Children's Centre*, (7)*University of Toronto*, (8)*Dalhousie University / IWK Health Centre*, (9)*Mount Allison University*

**Background**: Prospective studies have examined early expressive and receptive language development of high-risk infant siblings of children with ASD who later received a diagnosis of ASD ("ASD sibs"), relative to high-risk siblings who did *not* receive an ASD diagnosis ("non-ASD sibs"), and low-risk typically developing controls with no family history of ASD ("controls"). Cross-sectional analyses reveal impaired expressive and receptive language in ASD sibs by 14 months of age (e.g., Landa & Garrett-Mayer, 2006). However, evidence suggests that trajectory analyses may be more informative for risk than cross-sectional comparisons (e.g., Landa et al., 2013). Therefore, the current study sought to extend previous research by examining separate expressive and receptive language trajectories in a combined sample of ASD sibs, non-ASD sibs, and controls.

**Objectives**: The purpose of the current study was to examine early expressive and receptive language trajectories in high-risk sibs and low-risk controls relative to their 3-year diagnostic outcomes.

**Methods**: Data were derived from a Canadian multi-site prospective study of high-risk infant siblings of children with ASD. Participants were 523 children (371 high-risk sibs, 56% male; 152 low-risk controls, 52% male) followed from 6 or 12 months of age to 36 months of age. Based on independent, best-estimate clinical diagnoses at 36 months of age, participants were classified as ASD sibs (n = 94; 69% male), non-ASD sibs (n = 277; 52% male), or controls (n = 152; 52% male). Expressive and receptive language trajectories were examined based on corresponding standard scores on the *Mullen Scales of Early Learning* (*MSEL*) at 6, 12, 24, and 36 months. In the combined sample of high-risk and low-risk infants, semi-parametric group-based modeling was used to identify distinct trajectories that provided optimal fit to variation in *MSEL* standard scores over time.

**Results**: A 3-group solution provided optimal fit to the variation in both expressive and receptive language. The three trajectories within each language domain were characterized by the following patterns of scores: (1) inclining from average to above average, (2) stable-average, and (3) declining from average to below average. Trajectory membership was examined relative to 3-year diagnostic outcomes using Chi-square analyses ($p$'s < .001). For expressive language, ASD sibs were most likely to be members of trajectory group 2 (56.4%) or 3 (33.0%), with the remainder (10.6%) in group 1; non-ASD sibs were most likely to be in group 2 (53.8%) or 1 (39.0%), and controls were most likely to be in group 1 (69.1%) or 2 (28.3%). Similarly, for receptive language, ASD sibs were mostly members of trajectory group 2 (45.7%) or 3 (43.6%); non-ASD sibs were most likely in group 2 (53.4%) or 1 (40.4%), and controls were most likely in group 1 (68.4%) or 2 (45.5%).

**Conclusions**: Membership in the inclining, stable-average, or declining trajectories in both expressive and receptive language was related to 3-year diagnostic outcomes. Although ASD sibs, non-ASD sibs, and controls were in each trajectory group, membership in a declining trajectory (either expressive or receptive) was associated with a diagnosis of ASD.

**169.003** Longitudinal Trajectories of Language Development in Infants and Toddlers with ASD.

S. Paterson*[1], J. J. Wolff[2], J. T. Elison[3], N. Marrus[4], H. Gu[5], J. N. Constantino[4], A. M. Estes[6], H. C. Hazlett[2], J. Pandey[1], J. R. Pruett[4], R. T. Schultz[1], L. Zwaigenbaum[7], J. Piven[2], K. N. Botteron[8] and .. The IBIS Network[9], (1)*The Children's Hospital of Philadelphia*, (2)*University of North Carolina at Chapel Hill*, (3)*University of Minnesota*, (4)*Washington University School of Medicine*, (5)*UNC Chapel Hill*, (6)*University of Washington*, (7)*University of Alberta*, (8)*Washington University School of Medicine in St. Louis*, (9)*Autism Center of Excellence*

Background:

Delays in language and communication skills are common in young children who go on to develop Autism Spectrum Disorder (ASD). However, only a few studies have examined change in language skills longitudinally over early development or studied the predictive relationship between early language behaviors and later outcomes (see Charman et al., 2003; Ozonoff et al, 2010). In a cross-sectional study of 18 to 33 months olds, Luyster and colleagues (2008) found that non-

verbal cognitive ability, number of gestures, and response to joint attention contributed to receptive language variance, while non-verbal cognition, gestures, and imitation accounted for variance in expressive language.

Objectives:

First, we aimed to characterize developmental trajectories of receptive and expressive language in high-risk infant siblings who go on to develop ASD, those who do not, and in typically developing controls. Second, we sought to extend the work of Luyster et al. (2008) by investigating which aspects of early cognitive skills and language best predict language skills at 24 months.

Methods:

205 infants with older siblings with ASD (HR) and 78 infants with typically developing older siblings (LR) were assessed longitudinally as part of a larger, multi-site, study of brain and behavioral development in ASD. Language was assessed at 6,12 and 24 months using the Mullen Scales of Early Learning, Vineland Adaptive Behavior Scales and at 12 and 24 months using the MacArthur Bates Communicative Development inventory (M-CDI). Receptive and expressive language composite scores were calculated using a mean of receptive or expressive language scores respectively from the Mullen, VABS and the number of words understood or produced on the M-CDI. Autism outcome was determined at 24 months using the ADOS and clinical best estimate.

Results:

Data were analyzed for 3 groups of infants: low-risk controls with no ASD diagnosis (LR-), high-risk siblings with an ASD diagnosis (HR+) and HR siblings without ASD (HR-). Longitudinal analyses of trajectories for expressive and receptive language composites were conducted using linear mixed models. Analyses revealed that groups began to diverge at 12 months, with the HR+ showing significantly slower growth than the other two groups in receptive, $F(4,335) = 23.68$, $p<.01$, and expressive, $F(4,339) =10.09$, $p<.01$, language. The contribution of late and early gestures from the M-CDI, motor skills, and visual reception from the Mullen at 12 months to language performance at 24 months was examined using multiple regressions. For both expressive and receptive language outcomes, the number of gestures produced at 12 months had the greatest contribution to variance at 24 months, after controlling for socioeconomic status irrespective of group.

Conclusions:

Our longitudinal analyses confirm that differences in language performance emerge at around 12 months in HR infants who go on to develop ASD. It appears that early non-verbal communication skills make an important contribution to later language skills in infants at risk for ASD. Early deficits in these foundational language skills may be an important marker for later delays and offer an actionable target for early intervention.

**169.004** Early Predictors of Expressive and Receptive Vocabulary in Initially Nonverbal Preschoolers with ASD. P. J. Yoder*[1] and L. R. Watson[2], (1)*Vanderbilt University*, (2)*University of North Carolina at Chapel Hill*

Background:

Between 24 – 30% of children with autism spectrum disorders (ASD) do not use spoken communication by 5 years old. Spoken communication at 5 years predicts later adaptive outcomes in individuals with ASD. Identifying parsimonious predictive models of theory-guided predictors of vocabulary growth moves us towards understanding the variability in learning to communicate via speech within the ASD population. Parsimonious models include only predictors that account for significant variance in the outcome after statistically controlling for other predictors.

Objectives:

The incremental validity of eight putative predictors of growth curves of parent-reported expressive and receptive vocabulary was tested. Each putative predictor had empirical and theoretical grounds for selection.

Methods:

Eight-six initially nonverbal preschoolers with ASD were assessed 5 times in 4-month intervals over 16 months. Receptive and expressive vocabulary sizes were estimated using a parent report (i.e.,

the McArthur-Bates Communicative Development Inventory, Words and Gestures). The Communication and Symbolic Behavior Scale, Early Social Communication Scales, Motor Imitation Scale, Mullen Early Learning Scale, 2 parent-child interaction sessions, the Developmental Play Scale, and an oral motor assessment were used to measure putative predictors. Mixed level modeling was used to quantify individual vocabulary growth curves. The Time 5-centered intercept was selected as the parameter of interest because it is arguably the most interpretable parameter when quadratic or cubic models are needed to model growth (i.e., the best estimate of vocabulary size at Time 5). Putative predictors were measured at Times 1 or Time 2. To afford interpretable effect sizes, ordinary least square estimates of the intercepts for the growth curves were analyzed as the criterion variables in multiple regressions used to identify unique predictors (i.e., after controlling all other predictors in the model).

Results:

Quadratic models fit the data better than simple linear models. Except for IQ, all putative predictors predicted either expressive or receptive vocabulary. After controlling for other variables and after reducing the model to predictors with incremental validity, 3 predictors remained in each model. The number of parental linguistic responses to child leads at Time 2 ($R^2$ change = .12), number of intentional communication acts at Time 1 and 2 ($R^2$ change = .11), and number of different object play actions at Time 1 ($R^2$ change = .04) added to account for 29% of the variance (adjusted R square) in expressive vocabulary. The number of words understood at Time 1 ($R^2$ change= .27), number of object play actions at Time 1 ($R^2$ change = .10), and number of parental linguistic responses to child leads at Time 2 ($R^2$ change= .04) added to account for 49% of the variance in receptive vocabulary. Putative predictors without incremental validity were oral motor functioning, IQ, motor imitation, responding to joint attention, and consonant inventory.

Conclusions:

The results support selecting the unique predictors as goals for nonverbal children with ASD. The number of predictors, number of measurement periods, use of growth curves, long interval between predictor measurement and end-point of study, and large sample size make this study particularly important to the field.

**169.005** Persistence of Repetitive Behaviors in ASD. M. L. Cuccaro*, E. R. Martin, J. M. Lee, J. R. Gilbert and M. A. Pericak-Vance, *University of Miami Miller School of Medicine*

Background: Repetitive behaviors (RBs) are a defining feature of autism spectrum disorder (ASD) and have been studied extensively over the past decade (Leekam 2011). The use of RBs as a phenotype in genetic studies of ASD has expanded beyond an overall score (Cuccaro 2003; Szatmari 2006) but remains somewhat limited (Shao 2003; Smith 2009). Given evidence for trajectory of symptoms as an important phenotype in various diseases, exploration of change in RBs may represent a novel way to incorporate RBs into genetic studies of ASD.

Objectives: The primary objective of this study is to examine the pattern of changes in RBs using two empirically identified repetitive behavior factors, *Insistence on Sameness (IS)* and *Repetitive-Sensorimotor Behaviors (RSMB)*. The goal of this study is to determine whether change in RBs constitutes a viable phenotype.

Methods: Our dataset consisted of 989 unrelated individuals with ASD ranging in age from 48-239 months (M=116 months, sd=50) who were participants in a larger study of autism genetics. The sample was predominantly male (84%). The primary data for analysis consisted of 13 items from the ADI-R Interests and Behavior section and one item from the Language and Communication Functioning section (Verbal Rituals). For each item, Ever and Current ratings were used to develop the change score (i.e., Change=Current-Ever). Composite scores were calculated for IS and RMSB. Change scores for these composites served as our primary outcome of interest. Given the scoring convention used in the ADI-R, change scores reflect only whether current behavior has improved. Age, sex, language level, and adaptive level were incorporated into our analyses. Descriptive data for repetitive behavior items and composites were generated. To test for differences in degree of change for the respective composite scores we used a mixed models approach.

Results: Among the 14 RBs, the most frequently occurring (based on Ever ratings) were Repetitive

Use of Objects (83%), Undue General Sensitivity to Noise (79%), and Unusual Sensory Interests (76%). At the item level, the most change was observed for Repetitive Use of Objects (48%) while the least change was noted for Resistance to Trivial Changes in the Environment (14%) and Unusual Preoccupations (16%). We tested the association of age, sex, and adaptive level on our composite scores of interest (i.e., changes in IS and RSMB) and found that age at exam was significantly associated with both change in IS and RSMB; however, sex showed no association to change in IS but was significantly associated with the RSMB change score. Similarly, adaptive level was significantly associated with the IS changes score but not RSMB. Using a mixed model approach and adjusting for sex, age at exam, and adaptive level, we found no differences in the amount of change in IS and RSMB.

Conclusions: Change in repetitive behaviors vary across the different types of repetitive behavior. This preliminary analysis sheds light on patterns of change in RBs in ASD that may be useful in developing novel phenotypes. Certainly, the role of age, sex, and developmental level are critical influences on such phenotypes.

**169.006** Emerging Patterns of Repetitive Behavior Linked to Clinical and Behavioral Outcomes in High-Risk Infant Siblings. J. J. Wolff*[1], J. T. Elison[2], H. C. Hazlett[1], J. Pandey[3], S. J. Paterson[3], K. N. Botteron[4], A. M. Estes[5], L. Zwaigenbaum[6], J. Piven[1] and .. The IBIS Network[7], (1)*University of North Carolina at Chapel Hill*, (2)*University of Minnesota*, (3)*The Children's Hospital of Philadelphia*, (4)*Washington University School of Medicine in St. Louis*, (5)*University of Washington*, (6)*University of Alberta*, (7)*Autism Center of Excellence*

Background: Restricted and repetitive behaviors associated with autism spectrum disorder (ASD) were once believed to manifest after core social-communication symptoms. However, recent evidence suggests that such behaviors may be early manifestations of the disorder, emerging during a prodromal period in qualitatively different fashion than similar behaviors associated with typical development. How different forms of repetitive behaviors unfold during this early interval, particularly among toddlers at high familial risk for ASD, remains unclear.

Objectives: 1) Characterize early longitudinal profiles of repetitive behavior in a large, prospective study of infants at high familial risk for ASD (by virtue of having an older sibling with the disorder) and low-risk controls; and 2) Examine how early repetitive behaviors relate to key cognitive and behavioral outcomes.

Methods: Prospective, longitudinal parent-report repetitive behavior data (Repetitive Behavior Scales-Revised) were collected for 184 toddlers at high-risk for ASD and 59 low-risk controls at 12 and 24 months of age. Forty-two high-risk toddlers were classified with ASD at age 2 based on clinical best estimate by experienced, licensed clinicians. Longitudinal profiles of repetitive behavior across 5 subtypes were compared between groups using generalized estimating equations. The relationship of repetitive behaviors to cognitive and behavioral variables (e.g. ratio IQ, adaptive behavior, ASD symptom severity) were examined using nonparametric correlations.

Results: Longitudinal profiles for children with ASD differed significantly between groups on RBS-R composite and all subtype measures of repetitive behavior, $p < .0001$. High-risk toddlers without ASD were intermediate to low-risk and ASD positive counterparts. Cross-sectionally, toddlers who went on to meet diagnostic criteria for ASD showed significantly higher rates of repetitive behavior across repetitive behavior subtypes at the 12 month time point. Repetitive behaviors at 12 months predicted social communication scores and symptom severity at 24 months, and 12-month-olds with 3 or more forms of repetitive behavior were at four-fold risk for meeting diagnostic criteria at age 2. In children with ASD, repetitive behaviors were significantly negatively correlated with adaptive socialization scores. In contrast to findings from studies of older children with ASD, repetitive behaviors were unrelated to general cognitive ability in our sample of toddlers.

Conclusions: These findings suggest that as early as 12 months age, a broad range of repetitive behaviors are highly elevated in children who go on to develop ASD relative to both low-risk children and, importantly, high-risk counterparts who do not develop the disorder. While some degree of repetitive behavior is expected in typical early development, the nature and extent of these behaviors among toddlers who develop ASD appears highly atypical.

**169.007** Developmental Trajectories of Behavioural Symptoms in ASC. B. Lopez* and L. Over, *University of Portsmouth*

Background: Although seventy years have passed since Kanner (1943) first described autism, the exact nature of this spectrum of conditions still remains unknown. The failure to develop a full understanding of autism can be partially explained by the continuing lack of information still available on how autism develops over time. There are two main reasons for this neglect. First, the recognition that autism has a strong genetic component has resulted in an implicit tendency to conceptualise autism as a static condition with symptoms that remain pretty stable across time. Second, the major current theories of autism such as Theory of Mind, Executive Function or Weak Central Coherence are heavily weighted towards explanations of primary cognitive deficits, believed to have a genetic origin, and not explanations of *developmental* interactions between domains of ability/impairment. Yet autism is defined as a *developmental* disorder and hence any explanation of autism necessarily needs to incorporate a developmental component.

Objectives: The aims of this study were twofold. First the study aimed to map developmental trajectories of social impairments, repetitive behaviours and sensory behaviours in children with ASC. Second, the study aimed to explore developmental interrelationships between the three areas of impairments.

Methods: The parents of thirty-six children with ASC aged between 6 and 16 years of age completed the Repetitive Behaviour Questionnaire-2 (RBQ-2; Leekam et al, 2007), the Social Responsiveness Scale (SRS; Constantino and Gruber, 2005) and the Short Sensory Profile. Autism severity was measured by the Childhood Autism Rating Scale, Second Edition (CARS 2; Schopler et al, 2010) in 27 of the children and, for 8 children, it was measured with the Autism Quotient (Auyeung, Baron-Cohen, Wheelwright & Allison, 2008). The protocol for the study received ethical approval from the University of Portsmouth Ethics Committee which follows the guidelines of the British Psychological Society.

Results: The results showed differential trajectories for each area of behaviour relative to chronological age. Social difficulties remained relatively stable across the age range. In contrast developmental changes were observed in sensory behaviours, repetitive behaviours relating to Insistence of Sameness and repetitive sensory-motor behaviours. In terms of developmental interrelationships, while the development of social and sensory impairments seem closely linked, the development of repetitive behaviours seems to be relatively independent to the development of impairments in the two other domains.

Conclusions: The results demonstrate that while some behavioural symptoms change over the life span others remain stable. These findings have important implications for our conceptualisation of ASC. First, the results raise the possibility that while social impairments have a strong genetic component and are therefore impervious to environmental influences, the development of impairments in the two other areas may be successfully influenced by interventions. Second, the possibility that some areas of impairment in autism, in particular Insistence of Sameness, may be a 'side-effect' of genetic difficulties in other areas and note core to ASC will also be discussed.

**169.008** Longitudinal Associations Between Loneliness and Depressive Symptoms in Adolescents with ASD. R. E. Adams*[1], S. L. Bishop[2], B. K. Fredstrom[1], K. Gotham[3] and C. Lord[4], (1)*Cincinnati Children's Hospital Medical Center*, (2)*Center for Autism and the Developing Brain, Weill Cornell Medical College*, (3)*Vanderbilt University*, (4)*Weill Cornell Medical College*

Background: Adolescents with ASD report high rates of loneliness (Bauminger & Kasari, 2000; Bauminger et al., 2003), suggesting that, as a group, these adolescents are sensitive to their peer difficulties. Research with typical adolescents has consistently found a relationship between peer difficulties and symptoms of depression.

Objectives: Given that adolescents with ASD experience high rates of loneliness and more peer difficulties than typically developing adolescents, we examined whether loneliness predicts depressive symptoms in adolescents with ASD.

Methods: Participants were drawn from an ongoing longitudinal study of individuals with ASD first diagnosed at age 2. Between the approximate ages of 18 and 22, participants capable of completing self-report measures (n=40) and their parents filled out yearly questionnaire packets. Packets at three of these time points included the Asher loneliness scale

and a measure of depressive symptoms (either the Child Depression Inventory or the Beck Depression Inventory). Across these three waves, measures of depressive symptoms were highly correlated ($r = .84$-$.67$, $p < .001$).

Results: Exploratory principal components analysis was performed on all 24 Asher items for data from each of the three time points. For each of these analyses, only one factor was consistently found across each of the time points. Confirmatory principal components analysis was conducted for the three items that comprised this factor and found a consistent factor at each time point (For each time point, eigenvalue > 2.15, > 71.7% of the total variance explained, and all items loadings > .82, and all alphas > .80). Analyses were conducted on the average of these items for each time point (i.e. I feel alone at school or work, I feel left out of things, I am lonely). Correlations indicated that time 1 loneliness was correlated with depressive symptoms at all three time points ($r_s > .43$, $p_s < .001$), time 2 loneliness was correlated with depressive symptoms at times 1 and 2 ($r_s > .49$, $p_s < .001$), and time 3 loneliness was not correlated with depressive symptoms at any time point. Multiple regression analyses tested the direction of these associations and found that loneliness predicted increases in depressive symptoms from time 1 to time 3 ($\Delta R^2 = .19$, $F = 12.58$, $p < .003$), but depressive symptoms did not predict changes in loneliness over the same period ($\Delta R^2 = .01$, $F = 0.20$, p ns). Finally, LCGM found a two class model to be the best fit for the data with one group reporting low levels of loneliness over all three years and the other group reporting high levels of loneliness over all three years. The consistently high loneliness group had higher levels of depressive symptoms than the consistently low loneliness group for each of the three years ($t_s > 2.34$, $p_s < .03$).

Conclusions: Across multiple types of analyses, the findings suggest a predictive link between loneliness and depressive symptoms in adolescents/young adults with ASD. This underscores the importance of addressing loneliness and other aspects of the peer world in interventions for internalizing issues in this group.

## 170 Services for ASD: From Initial Parental Concerns to Adult Care

*Organizer:* C. Kasari *UCLA*

**170.001** A Meta-Analysis Comparing Parent- and Therapist-Implemented Early Interventions for Children with Autism Spectrum Disorders. A. S. Nahmias*[1] and D. S. Mandell[2], (1)*University of Pennsylvania*, (2)*University of Pennsylvania School of Medicine*

**Background:**

Researchers and practitioners generally recommend that parents be involved in the early intervention (EI) programming for children with ASD (Lord & McGee, 2001). There is a lack of consensus, however, regarding the extent to which parents should be responsible for implementation. Involving parents as therapists has the potential to provide increased opportunities to improve the parent-child social relationship, foster the generalization of skills, and increase the active intervention a child receives. Despite the promise of parent-implemented interventions to improve outcomes for children with ASD, results of intervention trials have been inconsistent. For example, one recent randomized control trial of a parent-implemented intervention did not demonstrate significant benefit compared with services available in the community (Rogers et al., 2012), but large effects were observed when the same intervention was implemented primarily by therapists (Dawson et al., 2010). These results highlight a potentially important difference in the efficacy of parent and therapist-implemented interventions. However, to date, the relative efficacy of parent and therapist implemented programs have not been examined using meta-analytic techniques. Rather than counting up the number of significant findings (as in previous reviews), which can be dependent on sample size, this approach estimates the strength of findings based on the pattern of effect sizes.

**Objectives:**

To conduct a meta-analysis comparing the effects of parent- and therapist implemented EI on cognition, communication, social behavior, and adaptive behavior outcomes.

**Methods:**

Randomized trials and quasi-experimental studies of EI programs for children with ASD were identified through a systematic search of online databases (PsycInfo, Medline, Eric, and Proquest Dissertations and Theses), hand-searching relevant journals, and citation reviews.

Standardized mean difference effect sizes (Hedges' *g*) for parent- and therapist-implemented interventions were assessed in separate meta-analyses for cognitive, adaptive behavior, communication, and social outcomes. Overall effect sizes were estimated using random effects models. Parent- and therapist implemented interventions were compared using adjusted indirect comparisons (analysis of variance of mixed-effects models). Meta-regression was used to assess the potential influence of additional covariates.

**Results:**

Twenty-two studies were identified that compared an EI program to a control group; half of the interventions were primarily delivered by a therapist and half trained parents as therapists. Parent-implemented intervention groups demonstrated significantly better communication outcomes than children in control conditions (Hedges' $g = 0.2$). Therapist-implemented intervention groups demonstrated significantly greater cognitive, communication, social, and adaptive behavior outcomes compared to control conditions, with Hedges' *g* of 0.5, 0.4, 0.5, and 0.6, respectively. Therapist-implemented interventions had significantly better cognitive outcomes than parent-implemented ones, and reached a marginal level of significance for social and adaptive behavior outcomes. The results of the meta-regression indicated that adjusting the comparison of parent and therapist-implemented interventions for study and participant covariates did not significantly change the magnitude of the difference in effect sizes between the two types of interventions.

**Conclusions:**

These findings highlight both the important role of the therapist in facilitating improved outcomes for young children with ASD and suggest the need for improved parent-training practices.

**170.002** Title: The Relationship Between Treatment Attendance, Adherence, and Outcome in a Caregiver-Mediated Intervention for Low-Resourced Families of Young Children with ASD. T. Carr*[1], K. Lawton[2] and C. Kasari[1], (1)*University of California Los Angeles*, (2)*Nisonger Center*

Background: Families of lower socioeconomic status have been underrepresented in early intervention research for children with Autism Spectrum Disorders (ASD). The examination of barriers to intervention research participation has been studied in the broader psychotherapeutic field, but not specifically within ASD. Such research is especially important given the benefit of early intervention on long-term prognosis.

Objectives: The purpose of the study is to investigate barriers to participation by examining how family demographic factors (family income, parent education, ethnicity/race, stress etc.) predict treatment attendance and adherence in a caregiver-mediated intervention for young children with ASD. Furthermore, the study will examine whether treatment attendance and adherence predict outcome.

Methods: This study is a secondary analysis of a caregiver-mediated randomized controlled trial targeting core deficits of ASD including joint attention and symbolic play (Kasari et al., under review). Caregivers and their child with ASD were randomly assigned to a caregiver-mediated condition (CMM) in which parents received twice weekly in-home sessions or a caregiver education condition (CEM) in which parents were delivered the same intervention content, but in group lecture format. Demographic variables included parent education, ethnicity, family income, number of children in the family, and parent-reported stress. Treatment attendance was measured as the percentage of sessions attended over the course of the 12-week intervention period while treatment adherence was measured as the degree to which the interventionist rated the caregiver's involvement in treatment strategies. Treatment outcome was operationalized as the amount of time in seconds caregiver-child dyads were jointly engaged during a play interaction. Generalized linear regressions were modeled to examine 1) the influence of demographic variables on treatment attendance, 2) the influence of demographic variables on adherence, and 3) the influence of treatment attendance and adherence on dyadic joint engagement.

Results: 147 families were assessed and randomized to a treatment condition. 30 families dropped out of the study prior to attending any treatment sessions, 20 of which were in the CEM condition ($X^2=4.01$, $p < .05$). Preliminary analyses found 1) treatment attendance was predicted by an interaction between treatment

condition and number of children in the family, such that receiving CEM and having more children was predictive of lower attendance (β = -8.34, p<. 05); 2) higher levels of caregiver stress were predictive of greater treatment adherence (β = -.01,p < .05); and 3) receiving CMM and greater treatment adherence were predictive of longer joint engagement (β = 103.59, p<. 001; β = 124.4, p<. 001, respectively), while treatment attendance had no effect (β = 1.01, p=.223).

Conclusions: Preliminary results suggest some influence of demographic variables on treatment attendance and adherence. Furthermore, caregiver involvement was predictive of treatment outcome, while caregiver attendance was not. These results stress the importance of considering demographic variables in research design when considering barriers to treatment attendance and adherence, and call for further analysis of the potential mediating influence these factors may have on treatment outcome.

**170.003** The Social Infrastructure of Autism Treatments in Schools. E. McGhee Hassrick*[1] and K. Carley[2], (1)*University of Chicago*, (2)*Carnegie Mellon*

Background: Most children with autism spectrum disorders receive intensive educational interventions as their primary form of treatment. These treatments often require collaboration among school staff and between home and school, because children diagnosed with autism have difficulty transferring skills learned in one setting to another. This study investigated the socio-economic and organizational barriers that impacted the alignment of interventions for children diagnosed with ASD, both among school staff and between home and school interventions.

Objectives: This research study used innovative network techniques to develop a new approach to tracking 1) the delivery of autism interventions in differently configured schools and 2) the alignment of autism interventions across school and home settings. We provide two network maps that illustrate different school level configurations of autism interventions and 45 individual child network maps the illustrate the degree of overlap among interventions provided by school staff members, family members and external providers in each of the two school settings. While the ultimate goal is to design interventions that facilitate intervention alignment, for this study, our objective was to create a baseline measure of the degree of variance in intervention alignment among individual children situated in the same school, across socio-economic categories.

Methods: We conducted 200 hours of field observations that generated 600 pages of digital field notes, 31 semi-structured transcribed interviews and 90 network surveys with 90 school teachers, aides, clinicians and parents, about forty five children diagnosed with autism spectrum disorder, who were situated in two differently configured public schools in a large metropolitan area. The study employed a "saturation sample", which included recruitment of all parents of autistic children and all staff that provided interventions for those children at the two field sites. Interventions were rated as established, emergent or un-established using the National Standards Report (20009). Collection and analysis of qualitative data was done in tandem, allowing the development of working hypotheses, the adjustment of data collection strategies, and the pursuit of new data regarding interactions discussed in interviews and during observations. Coding categories were developed from theoretical review and analysis of interview and observational data. All interviews and observation notes were read several times, using memos, pattern coding, case analysis (across social class), and written summaries to aid in assuring the quality of data collection and provide opportunities for on-going data analysis. We used Dedoose to analyze the qualitative data. Parent and autism provider network survey data will be analyzed using ORA for dynamic, multi-modal networks and network visualization.

Results: Two school configurations were identified: 1) a "school-within-a-school" model and 2) a maximum inclusion model. Intervention network maps for low income children had fewer interventions rated at established or emergent, with lower levels of alignment in the "school-within-a-school", compared with the maximum inclusion model.

Conclusions: Preliminary findings indicate that school design may shape alignment of individual interventions for children diagnosed with ASD.

**170.004** Engagement of Students with ASD in Elementary and Middle School Classrooms. J. R. Dykstra*, *University of North Carolina - Chapel Hill*

Background:

Understanding engagement in the classroom setting is critical to providing effective educational programs for students with ASD. Joint engagement, which incorporates the social aspects of engagement and learning, may be particularly sensitive to the challenges of students with ASD. Although joint engagement has been examined in preschool children, it has not been examined in elementary and middle school students with ASD.

Objectives:

This descriptive study examines the joint engagement of students with ASD in classrooms in relation to other classroom and student variables. The specific objectives of this study were (1) to characterize student engagement in the classroom, (2) to examine the relationships between teacher and instructional factors and student engagement, (3) to examine the relationships between student characteristics and engagement.

Methods:

The participants for the study were recruited from 8 elementary and middle school self-contained classrooms (i.e., serve only children with disabilities). There were 25 student participants in the current study, with 2 to 4 student participants from each of the eight classrooms. All students had an educational label of autism and ranged from 8 to 12 years old at the time of recruitment.

The researcher conducted a series of observations and assessments to gather data for the study. The dependent variable, student joint engagement, included six hierarchical categories: unengaged, onlooking, object only, person only, supported joint engagement, and coordinated joint engagement (Adamson et al., 1998). Engagement data were collected using observational coding during one-to-one, small group and large group classroom instruction. The independent variables included teacher, instructional, and student characteristics. Teacher characteristics (interaction style and teacher burnout) were measured through observations and questionnaires. Instructional characteristics were measured using observational coding and included group size and use of student-directed practices. Student characteristics included expressive communication, receptive vocabulary, and autism severity, and were measured using standardized and semi-structured assessments.

Data for the current study were collected at three different levels: classroom, student, and observation. Based on the nested design of the study, the researcher used mixed level modeling for statistical analyses, with engagement being modeled as a function of different independent variables.

Results:

The students in the study were actively engaged approximately 40% of the time, and passively engaged or unengaged for around 60% of the time. The results showed that smaller group size and the use of more student-directed practices were significantly related to student joint engagement. Additionally, joint engagement was significantly related to expressive communication, but was not related to autism severity or receptive vocabulary. Joint engagement was not related to teacher characteristics.

Conclusions:

Based on extrapolation from the study and assuming a 30-hour school week, students in the study would be actively engaged for approximately 12 hours per week, well below the recommended 25 hours of active engagement for effective intervention with children with ASD (NRC, 2001). The findings of the study suggest that specific instructional practices may impact joint engagement in older students with ASD. Additionally, the relationships between joint engagement and specific student characteristics may have implications for educational programming or placements.

**170.005** Parent Developmental Concerns, Provider Response to Concerns, and Delayed Autism Spectrum Disorder Diagnosis. K. Zuckerman*, O. J. Lindly and B. K. Sinche, *Oregon Health & Science University*

**Background:** Early diagnosis of autism spectrum disorder (ASD) and other developmental disorders is associated with improved long-term outcomes. However, most children with ASD are not diagnosed until school-age. How health care providers elicit and respond to early parent developmental concerns may impact age of ASD diagnosis.

**Objectives:** Our objective was to assess whether age of first parent concern and first parent discussion of concerns with a provider differs in children with ASD versus intellectual disability/developmental delay (ID/DD), and to assess whether provider response to first parent concerns is associated with delayed ASD diagnosis.

**Methods:** Using data from the 2011 Survey of Pathways to Diagnosis and Services, we analyzed diagnostic experiences of 1420 children with ASD and 2098 children with ID/DD. We assessed three time points in the child's diagnostic experience: child age at first concerns, age at first conversation with a provider, and age at ASD diagnosis (for ASD group only). We also assessed how health care providers responded to parents' first concerns, via yes/no report of six provider actions, categorized into two domains (proactive vs. reassuring/passive). Using t-tests, we compared age of first parent concern, age of first provider conversation, and type of provider response in ASD versus ID/DD groups. Among children with ASD, we used logistic regression to test the association between provider response type with experience of diagnostic delay ≥3 years.

**Results:** Compared to children with ID/DD, children with ASD had lower mean age of first parent concern (2.12 vs. 2.99 years, p<0.001) and first discussion of concerns with a provider (2.33 vs. 3.24 years, p <0.001). Time between first parent concerns and first discussion of concerns with provider was similar in both groups (0.27 vs. 0.31 years, p = 0.61). Children with ASD were diagnosed at a mean age of 5.18 years (4.91–5.45) and experienced a mean delay of 3.05 years (2.79-3.30) from age at first concerns to age of diagnosis. Children with ASD were less likely than children with ID/DD to experience ≥2 proactive provider responses to parent concerns (AOR: 0.68 [0.50-0.90]) and were more likely to experience ≥1 reassuring/passive responses (AOR: 1.44 [1.09-1.91]). Among children with ASD, those with ≥2 proactive responses to parent developmental concerns were less likely to have a ≥3 year delay between first parent concern and ASD diagnosis (AOR: 0.53 [0.35-0.82]), or between first discussion with provider and ASD diagnosis (AOR: 0.43 [0.28 - 0.65]). In contrast, CSHCN with ASD having ≥1 passive/reassuring responses had higher odds of both these delays (AOR: 2.45 [1.62 - 3.69] and AOR: 2.53 [1.66 - 3.85]).

**Conclusions:** In this nationally-representative U.S. sample, children with ASD experienced significant diagnostic delays. Despite early parent concerns, children with ASD had less proactive and more passive provider responses to first parent concerns than children with ID/DD. Less proactive/more passive provider responses were associated with diagnostic delays in ASD. Findings highlight the need for stakeholders and policyholders to provide more support to front-line health care providers, so that children with ASD receive early access to evidence-based care.

**170.006** Planning for the Future: The Service and Care Needs for Adults with Autism Post Parental Care. V. D'Astous*[1], K. F. Glaser[2] and K. Lowton[3], (1)*Home*, (2)*Institute of Psychiatry, King's College London*, (3)*King' College London*

Background:

Research has shown that the complex disabilities of autism persist across the life course (Hare et al., 2004). Adults with autism experience multiple challenges with communication, socialization, learning, self-help, independent living and adaptation to change (Happé and Charlton, 2012). Research has highlighted limitations in service provisions and availability for adults with autism with family members providing and maintaining supportive needs across the lifespan (Hare et al., 2004; Gerhardt and Lainer, 2011). The continuation of supportive services across the life course for individuals with autism is thought to be critical for their wellbeing. At some point in their lives most adults with autism are likely to experience the transition out of their parents' care, requiring alternative residential and supportive services. There is a lack of research considering what future care service and support needs adults with autism will require to successfully manage this transition.

Objectives:

To explore from a holistic family perspective (adult with autism, parent carer and adult sibling) the service and support needs, family roles and relationships and long term care plans in families with an adult with autism.

Methods:

This research builds on an earlier study that collected information on the characteristics and service use and needs of individuals with autism as they transitioned into adulthood. Stage one uses quantitative questionnaires to acquire a comprehensive view of the caregiver and the adult with autism's mental and physical abilities, and to assess their needs and service use (n=100 families). Stage two uses face-to-face semi-structured individual interviews with a subsample (n= 30 families) to explore family relationships, role changes, concerns, preferences and future expectations for caregiving from three family member perspectives (adult with autism, parent carer and adult sibling). Furthermore, a comparative analysis of two cohorts of older caregivers (55-64 and 65 or over) may highlight disparities in historical and social experiences and provide insight into the differences and similarities in service needs and future care planning for an adult family member with autism.

Results:

Adults with autism have high levels of unmet service needs. Parent caregivers, adults with autism and their siblings all worry about the future. Preliminary data records fears of change, wellbeing and isolation, and concerns of high exploitation risks, limited daily living skills and social interactions. A lack of knowledge about options and availability of services appears greater among older parent caregivers. Future care plans seemed to be largely informal agreements with siblings assuming a variety of roles.

Conclusions:

This study begins a dialogue of acceptance of this transitional eventuality and the benefits of future care planning to create a secure future in which the health, housing and social care needs of an adult with autism are considered and designed to ensure their continuity of wellbeing. Adults with autism and their families require more care and supportive services, and information to assist them in future planning.

**170.007** Perspectives of Youth with ASD on Social Competence, Friendships, and Intervention. K. M. Bottema-Beutel*, *Lynch School of Education, Boston College*

Background: Secondary students with ASD experience difficulty in managing the social context of schools, including interactions with peers and school staff, accessing social activities, and meaningfully participating in the classroom (Humphrey & Lewis, 2008). Difficulty in developing friendships can leave adolescents with ASD on the fringes of social life (Locke et al., 2010; Wagner et al., 2004). They may be involved in fewer friendships, meet less frequently with friends, experience poorer friendship quality, and form friendships that are of shorter duration than peers without ASD (Bauminger and Kasari, 2000; Bauminger and Shulman, 2003; Calder et al., 2012; Kasari et al., 2011; Locke et al., 2010). To mitigate these outcomes, school-based interventions have been designed to improve social competence and provide greater access to experiences with typically developing peers in an effort to promote social relationships (Carter et al., 2012; Koegel et al., 2012; Stichter et al. 2010). Understanding the perspectives of youth with ASD in regards to these practices can help researchers and practitioners optimize intervention practices.

Objectives: To determine the perspectives of youth with ASD in regards to social success, friendships, and intervention components aimed at improving social competence and promoting peer relationships.

Methods: We conducted interviews with 33 youth with ASD to gather their views on social success, friendships, and eight intervention components: 1) Identifing social goals, 2) Recruiting peers, 3) Holding an orientation meeting, 4) Meeting with peers, 5) Adult assistance, 6) Social skills instruction, and 7) Family Involvement. We also presented possible variations on each component. TTo maximize comfort with the interview process, participants were given a choice of in-person, video chat, over the phone, email, and instant message formats. Adaptations were used during the interview process (i.e., visual supports) to maximize input from participants with language difficulty. Interviews were transcribed in full and analyzed qualitatively. An inductive, iterative coding process was applied to develop themes and categorize interview responses.

Results: The majority of participants viewed social success and friendships as important and responded favorably to most of the intervention

components. However, they expressed concern about particular intervention strategies. Several themes emerged, including the negative effects of adult intrusion into adolescent social life, the relevance of social skills, a preference for learning through enjoyable activities with peers, and ambivalence about the disclosure of disability status, as it could lead to either increased understanding or further stigmatization.

Conclusions: Service providers and intervention researchers in secondary settings should take into account the preferences of students with ASD when planning socially-focused interventions, including the role of the adult, the intervention format, and disclosure of disability status. Adults should consider whether the kinds of interactions they are arranging, the steps they take to facilitate interactions, and the skills they promote violate or promote the social norms of the participants involved. Failure to design intervention contexts that are viewed by the participants as relevant and worthwhile in their social life may undermine intervention efforts.

**170.008** The cost effectiveness of ESDM. D. S. Mandell*[1], Z. Cidav[2], J. Munson[3], A. Estes[3] and G. Dawson[4], (1)*University of Pennsylvania School of Medicine*, (2)*Center for Mental Health Policy and Services Research, University of Pennsylvania*, (3)*University of Washington*, (4)*Duke University*

Background: A number of intervention programs for very young children have been developed that demonstrate remarkable efficacy in improving cognition, social interaction and adaptive behavior. These interventions are very expensive to implement, however. Concerns have been raised about their cost effectiveness and place within the healthcare system and publicly funded education system. In response, a number of simulations have been published, suggesting that children who receive intensive early intervention will have lower societal costs, especially in their use of medical and educational services over the lifespan. None of these simulations has contained data from a cohort of children who have received these interventions, however, nor have those been compared with data from children who did not receive one of these evidence-based interventions.

Objectives: to examine the cost effectiveness of one such intervention, the Early Start Denver Model (ESDM)

Methods: Data were obtained from the original randomized controlled trial of ESDM. Service use data were collected on all children in the trial during the intervention period and for four years post intervention. Weekly service use was calculated in multiple categories and included the intervention itself (ESDM), early intensive behavioral intervention, functional therapies, special education, parent training, social skills training, general education, and other costs. Services were monetized by pooling data from previous studies. Costs were log transformed to normalize the distribution. T-tests were used to assess the statistical significance of differences in cost between the intervention and control groups.

Results: Analyses are ongoing. Preliminary results suggest that during the intervention period, service costs for the intervention group averaged approximately $10,000 per child, compared with $5300 for the control group. Post intervention, service costs for the intervention group averaged approximately $4400 per child, compared with $5600 in the control group. Differences in cost post intervention were especially apparent in use of early intensive behavioral intervention and special education services. Return on investment occurred approximately 10.5 years post intervention (i.e., when most subjects would be entering high school). That is, accrued costs were equal between groups at that point, and were projected to be higher for the control group than for the intervention group after that point.

Conclusions: The results suggest that the cost effectiveness of ESDM is realized much earlier in the lifespan that would be projected from prior simulation studies. Of note, the current study did not include many other direct and indirect costs whose inclusion could have greatly increased the observed difference between groups. Challenges faced in analyzing these data suggest the need for easy-to-complete service use and cost instruments that are included as part of intervention trials.

## 171 Animal Models

**171.001 1** Endogenous Retrovirus Expression in Two MOUSE Models of Autism Spectrum Disorders. L. Ricceri*[1], E. Balestrieri du Marteau[2], A. De Felice[1], C. Matteucci[2], A. A. Dendoba[2], C. Cipriani[2], M. L. Scattoni[1], G. Calamandrei[1] and P. Sinibaldi-Vallebona[2], (1)*Istituto Superiore di Sanità*, (2)*University of Rome Tor Vergata*

Background: Mobile retroelements such as Human Endogenous Retrovirus (HERV) have been implicated in many complex diseases with multifactorial etiology and genetic basis, including neurological and neuropsychiatric disorders. In a previous study we demonstrated that specific HERV families show a distinctive expression profile in peripheral blood mononuclear cells (PBMCs) from Autistic Spectrum Disorders (ASD) patients compared to healthy controls, suggesting that HERV expression may contribute to etiopathogenesis of this complex disease.

Objectives: We evaluate the expression profile of different mouse endogenous retrovirus (MERV) families in mouse models of ASD to investigate their potential role in the etiopathogenesis of the disease. Two different ASD mouse models were selected. The first model was fetal exposure to valproic acid (VPA) in outbred mice. VPA is an antiepileptic drug used also for the therapy of bipolar disorders; prenatal VPA exposure in humans is associated with a 7-10x increase in relative risk for ASD, whereas prenatally VPA exposure in mice leads to autism-like anatomical and behavioral abnormalities in the offspring. The second model was the inbred mouse line BTBR T+tf/J (BTBR) that shows behavioral abnormalities analogous to the core ASD symptoms.

Methods: We used CD-1 outbred mice prenatally exposed to VPA by subcutaneously injection of a single dose of VPA (500mg/Kg) at gestational day 12.5 and BTBR mice. Behavioural analysis was carried out in developing and adult VPA exposed mice. In both mouse models, blood and brain samples were collected at different postnatal days and relative quantification of several MERV families (ETnI, ETnIIα, ETnIIβ, ETnIIγ, MusD and IAP) were done by Real-time PCR. Standard analysis of variance was applied to assess differences between each group and its control.

Results: VPA exposed mice showed a delay in acquisition of neonatal motor patterns and reduction of explorative activity at weaning. In blood samples relative expression of MERV families (ETnIIα, ETnIIβ, ETnIIγ, MusD and ETnI) was higher in VPA treated than in controls at all the time of observation (postnatal days 1, 7 and 23). In the brains, MERVs expression differences between VPA treatment and controls were even more evident than in corresponding blood samples. The same enhanced expression profile of MERV was found in the BTBR line: in blood samples and in brain homogenates, relative expression of ETnIIalpha, ETnIIbeta, ETnIIgamma, MusD and IAP, ETnI, and IAP was higher than in controls (C57BL/6j), indicative of higher MERV expression.

Conclusions: Data obtained from blood and brain samples from both BTBR and VPA mouse models support the hypothesis that an increase of the MERVs expression can be associated with the ASD-like behavioural phenotype. These results are in agreement with what we previously described in autistic children. Interestingly the MERV expression profile observed in brain samples from both ASD mouse parallel the one blood samples. The high levels of expression found in brain pave the way for further studies aimed to clarify whether the different profile of MERV is associated with neuroinflammation and encourage us to verify if drug treatments targeting MERV expression may modify or revert the ASD phenotype.

**171.002 2** A Mouse Model of Prenatal Vitamin D Deficiency: Effects on Offspring Behavior, Systemic Immune and Gut Microflora Profiles. K. L. Jones*[1], A. M. Belenchia[2], V. Vieira-Potter[2], C. A. Peterson[2], M. J. Will[2] and D. Q. Beversdorf[2], (1)*University of California - Davis*, (2)*University of Missouri*

**Background:** Vitamin D deficiency/insufficiency, defined as inadequate circulating concentrations of 25-hydroxyvitamn D (25OHD), has been estimated to affect up to 75% of pregnant women in some developed nations. Multiple studies have established an associative link between low maternal 25OHD concentrations and a variety of mental health conditions, including autism spectrum disorders (ASD).

**Objectives:** The current study aimed to examine the effects of prenatal vitamin D deficiency on offspring behaviors. Additionally, as immune and gastrointestinal dysregulation is seen in some individuals with autism, we examined the effect of prenatal vitamin D deficiency on immune and gut microflora profiles in offspring.

**Methods:** Female C57BL/6J mice were assigned to either a vitamin D deficient diet or a control diet two weeks prior to mating and maintained on this diet throughout pregnancy until postnatal day 7, at which point both dietary groups were switched to the control diet. We subsequently

recorded the ultrasonic vocalizations of the offspring on postnatal day 8 as a measure of social communication. Beginning on postnatal day 60, the adult offspring were tested for levels of social interaction using the Crawley 3-chamber social approach task. Anxiety was tested using the elevated-plus maze, and general activity levels were assessed using the open field. Offspring were euthanized after the completion of behavioral testing, at which time serum, white adipose tissue, liver, intestines, and quadricep were collected from all male offspring. Offspring serum was tested for eight immune analytes to examine if prenatal vitamin D status had long lasting effects on general systemic inflammation. Adult offspring intestinal microbiota was analyzed for microflora profiles, examining a variety of different microfloral species.

**Results:** There were no differences in behavior between offspring prenatally exposed to the vitamin D deficient diet and control offspring. Out of eight immune analytes measured, the vitamin D deficient offspring had significantly higher levels of the proinflammatory markers resistin and IL-2 than control offspring. Further, vitamin D deficient offspring were found to have a significantly altered gut microflora profile than that of control offspring.

**Conclusions:** These results suggest that despite emerging theories, it does not appear that prenatal vitamin D deficiency leads to the development of autistic-like behaviors in offspring, However, is important to note that prenatal vitamin D deficiency may lead to abnormalities in behaviors not tested in the current study. Despite no changes in behavioral profiles between groups, prenatal vitamin D deficiency does appear to have long lasting consequences on systemic immune and gut microflora profiles in adult offspring. Further research is needed to determine whether prenatal deficiency leads to other cognitive and behavioral deficits in offspring as well as any other long-lasting physiological differences.

**171.003 3** Activity-Dependent Changes in Microtubule-Dependent Synaptic Transport in an Animal Model of Autism. S. Uchida and G. P. Shumyatsky*, *Rutgers University*

Background: Activity-dependent changes in the brain include various processes at the synapse, cell body and nucleus as well as an increase in their communications, which is mostly served by cytoskeletal structures, microtubules and actin filaments. Contrary to the previous view that microtubules are stable in mature neurons, we find that microtubules change their stability following behavioral activity. We also find that a microtubule inhibitor, stathmin, controls these changes in microtubule stability in response to activity.

Objectives: We tested the hypothesis that activity-dependent changes in dentate gyrus microtubules may lead to changes in synaptic transport that lead to ASD-related behavioral phenotype.

Methods: We have generated Stat4A mutant mice where stathmin expression is controlled by tetracycline-dependent tTA system. In the hippocampus, Stat4A mice have strong expression in the dentate gyrus. We will test these mice in several social and cognition behaviors related to ASD.

Results: Stat4A mice show deficits in affiliative behaviors (maternal pup retrieval), anxiety and motivation. There is increasing evidence suggesting that autism and maternal depression and deprivation are linked. More specifically, the environment, both prenatally and during early postnatal life is a significant factor in the development of psychiatric disorders, including autism, in offspring (Gilbert et al., 2009; Green et al., 2010; Feldman, 2012; Oh et al., 2013). The Jan and Jan group has shown that pups' interactions with their mother strongly influence the pup's vocal communication, ultrasonic vocalizations (USV) (Young et al. 2010). We will next test USV in pups born and raised by Stat4A mothers as deficits in USV have been found to be indicative of behaviors similar to ASD in humans. If we find these changes it will be consistent with social communication deficits in autism.

Conclusions: Our current results suggest that dentate gyrus microtubules controlled by stathmin are involved in behaviors related to ASD. Therefore, Stat4A mouse may be a useful animal model for ASD.

**171.005 5** CNTN4, a Candidate Gene Associated with Autism Spectrum Disorders and Anorexia Nervosa, Has a Function in the Neurodevelopmental Trajectory of Cognitive Rigidity in Mice. A. Oguro-Ando*, R. Molenhuis, L. de Visser, J. J. Sprengers, P. H. Burbach and M. J. Kas, *Brain Center Rudolf Magnus, University Medical Center Utrecht*

Background: Cognitive rigidity is a major clinical relevant characteristic of various psychiatric illnesses, including autism spectrum disorders (ASD) and anorexia nervosa (AN). Understanding the developmental trajectory of neurobiological mechanisms underlying cognitive rigidity will be an important step to develop clinical treatment that may be relevant across these different psychiatric diagnoses. Both ASD and AN have a multifaceted symptomatology, however, they have overlapping features with respect to restricted behaviors and behavioral inflexibility. *CNTN4* (contactin-4) codes for a cell-adhesion molecule gene that has recently been linked to both ASD and AN.

Objectives: To investigate on how *CNTN4*-deficiency may modulate brain development and behavior, we used a *Cntn4* gene knockout mouse model to determine how CNTN4 protein contributes to cortical development and behavior. The approach permits empirical evaluation of how variation in *CNTN4* may act to modulate risk and presentation in patients with deletion who have classic autism. We have begun to perform behavior analysis and a morphological characterization using mouse model.

Methods: We assessed a wide variety of health measures, behaviors and cognitive capacities in *Cntn4* KO, heterozygous and wild type mice. In addition, Nissl and Golgi stainings of cortical neurons were analyzed for morphological analysis and reconstruction of dendritic arbors by manual tracing (Neuro Lucida software).

Results: Our behavioral studies have shown that *Cntn4* KO and heterozygous mice made significantly more errors before reaching the criterion for intra-dimensional reversal learning (affective set-shifting) compared to wild type mice ($p < 0.05$; Student t-test). The mice also needed significantly more trials to complete this sub-task ($p < 0.05$; Student t-test). In contrast, no effect was found on odor detection or extra-dimensional (attentional) set-shifting. Moreover, no genotype effects were detected in the longitudinal assessment of health measures and other behavioral domains. Interestingly, brain morphology analyses revealed a significant reduction of cortical layer thickness in the motor cortex ($p < 0.05$; Student t-test), but not in non-frontal areas including somatosensory cortex and visual cortex.

Conclusions: Reversal learning is considered a core component of cognitive rigidity, a behavioral domain affected in both ASD and AN. Our behavioral and pathological results in *Cntn4* KO mice revealed a link between frontal cortical mechanisms and cognitive rigidity behavior. Together, these findings suggest that this mouse model is highly suitable to examine neurobiological underpinnings of cognitive rigidity in neurodevelopmental disorders. Ultimately, this approach may lead to the development of therapeutic strategies with cross-diagnostic relevance

**171.006 6** Cerebellar Stimulation Differentially Modulates Neuronal Activity in Mouse Prefrontal Cortex. Y. Liu[1], C. Blaha[2], G. Mittleman[2], D. Goldowitz[3] and D. H. Heck*[1], (1)*University of Tennessee Health Science Center*, (2)*University of Memphis*, (3)*University of British Columbia*

Background: There is no unique neuropathology associated with autism spectrum disorders (ASDs). However, the prefrontal cortex (PFC) and the cerebellum (CB) are two brain areas strongly implicated in ASD, suggesting that impaired cerebro-cerebellar communication may contribute to the development of ASD. Connections between the PFC and cerebellum have been found in primates (1) and Imaging studies suggest such connections also exist in humans (2). In mice electrical stimulation of the cerebellar dentate nucleus results in dopamine release in the PFC (3) but little is known how CB activity affects neuronal activity in the PFC.

Objectives: We investigated how electrical stimulation of the cerebellar cortex affects neuronal activity in frontal and prefrontal cortical areas in awake behaving mice.

Methods: We recorded local field potential (LPF) and single unit spike activity with up to five extracellular recording electrodes in the prelimbic, secondary motor and/or frontal association areas (Ant.-Post.: Bregma +2, Lat: 0.2 - 2.5 mm). Electrical stimulation (10 ms, 50 Hz, 100 μA, for 1.0 s) was applied with a bipolar electrode to the surface of the cerebellar hemisphere (Ant. Post.: -6.2, Lat.: 2 - 2.5 mm).

Results: At rest, the fluctuations of LFP activity were strongly correlated between recording sites and showed large, synchronized amplitude negative peaks at irregular intervals, which were associated with pauses in single unit spike activity

across multiple recording sites. Cerebellar stimulation eliminated negative LFP peaks for a period of a few to tens of seconds, depending on stimulus amplitude. We analyzed the responses of 229 single units to cerebellar cortical stimulation. Firing rate increased in 73 (31.9%) and decreased in 28 (12.2%) units with 128 units (55.9%) showing no change in firing rate following cerebellar stimulation. Unilateral cerebellar stimulation affected PFC neuronal activity bilaterally.

Conclusions: Our findings show that increasing cerebellar cortical activity via electrical stimulation differentially modulates LFP and spiking activity in awake mouse PFC neurons, resulting in a temporary desynchronization of PFC network activity, an effect that might involve dopamine transmission (3).

References:

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**171.007 7** Characterization of Mice Bearing Humanized Androgen Receptor Genes (h/mAr) Varying in Q Tract Polymorphism Length. Z. Buchwald*[1], J. Ellegood[1], C. Burton[1], D. M. Robins[2], A. Raznahan[3], P. D. Arnold[1] and J. P. Lerch[4], (1)*Hospital for Sick Children*, (2)*University of Michigan*, (3)*NIH IRP, NIMH, Child Psychiatry Branch*, (4)*University of Toronto*

Background: The androgen receptor (AndR) is a ligand-activated transcription factor that is crucial for male sexual development. AndR is linked to several disorders, including ADHD, Autism, and Androgen Insensitivity Syndrome. Mice bearing humanized AndR genes (h/mAr) with varying lengths of a polymorphic N-terminal glutamine (Q) tract have been created. The length of the Q tract is inversely proportional to the AndR activity, and therefore allows investigation of the affect of androgen on the behaviour and neuroanatomy.

Objectives: To determine the behavioural and neuroanatomical phenotype of the AndR mousseline, which can lead to a better understanding of the initiation, progression, and treatment of androgen related disorders, as well as sex-related differences, as AndR plays a crucial role in sexual behaviors.

Methods:

*Mice* – Three separate mouselines have previously been created with varying Q tract lengths (Albertelli et al. 2006), 12Q (short), 21Q (normal), and 48Q (long). Two separate cohorts of mice were used. The first cohort was naïve and sacrificed at P60 for MRI scanning; this cohort consisted of male hemizygotes, and female hetero- and homozygotes for each mouseline. The second cohort consisted of only male hemizygotes and were bred to ~P60 and subjected to 4 different behaviour tests, sacrificed and set to undergo further MRI scanning to examine brain/behaviour correlations

*MRI Acquisition* - Scan parameters: T2- weighted, 3D fast spin-echo sequence (TR - 2000 ms, TEs - 14 ms, 6 echoes, 2 averages, FOV - 14 x 14 x 25 $mm^3$, Matrix size = 250 x 250 x 450). This sequence yielded an image with 0.056 mm isotropic voxels (3D pixel). Total imaging time ~12 h (Lerch et al. 2011). The same sequence was used on both the naïve and behavioural tested cohorts.

*Behavioural Testing* - Tests were used to assess grooming (timed observation), anxiety (open field), sociability (3 chamber test), and compulsive behaviors (marble burying). Each test was performed per standard practices and no test was performed within 4 days of one another.

Results: *Volume* - Measurements revealed that the hemizygote 12Q and homozygote 48Q mice display the most volume differences compared to the WT, with the differences in the homozygote 48Q the most severe with 43 of the 62 regions found to be larger in size. The opposite was found in the hemizygote 12Q mice with 15 of the 62 regions smaller. *Behaviour* - Testing revealed that the 12Q mice groomed less compared to WT, indicating a lack of compulsive behavior. They spent more time in the center of the open field box, indicating a non-anxious phenotype. Behavioural results from the 48Q mice are forthcoming, and while these results are preliminary they indicate possible behavioral differences between the AndR mouselines.

Conclusions: The difference in Q tract length of the androgen receptor affects the brain differently in males versus females, with increase androgen activity causing decreases in the male brain and

decrease androgen activity causing increases in the female brain. Behavioural invesitigation revealed a possible role for androgen activity in both repetitive and anxiety related behaviours.

**171.008 8** Effect of Perinatal Asphyxia on Protein Expression in Rat Prefrontal Cortex during Postnatal Development. S. Lam[1], T. Wakuda[2], Q. Li[1], R. Wei[1], X. Zhang[1], P. C. Sham[1], Y. Wang[1], S. E. Chua[3], N. Takei[2] and G. M. McAlonan*[4], (1)*The University of Hong Kong*, (2)*Hamamatsu University School of Medicine*, (3)*University of Hong Kong*, (4)*Institute of Psychiatry, King's College London*

Background: Human epidemiological studies have linked labor and delivery complications leading to hypoxia/ischemia at birth with increased risk of neurodevelopmental disorders such as schizophrenia and autism. This can be modeled experimentally by exposing rat pups to 15 min of intrauterine anoxia during Caesarean section birth causing behavioral anomalies relevant to neurodevelopmental disorders such as autism. This model also affords us the opportunity to directly examine brain cellular mechanisms modified by this perinatal assault.

Objectives: To carry out a direct experimental test of the impact of perinatal asphyxia on protein expression in the postnatal prefrontal cortex.

Methods: We used two dimensional differential in-gel electrophoresis and mass spectrometry, with targeted western blot analyses for confirmation, to quantify the proteomic profile of the prefrontal cortex - a region strongly implicated in autism - in 6 (adolescent) and 12 (adult) week old rats previously exposed to perinatal asphyxia. Control groups included pups delivered by C-section without anoxia and pups delivered vaginally. Group differences in global protein expression were examined using a partial least squares discriminative analysis ( SIMCA 9.0 software, Umetrics, Sweden; PLS-DA) and the expression differences of individual proteins examined using Analysis of Variance run on Progenesis software (initial screen across all groups, significance threshold set at $p < 0.1$; post-hoc analysis of group contrasts, significance threshold set at $p < 0.05$). Finally western blot was used to confirm gel-differences in selected proteins.

Results: Multivariate analyses of protein spots present in at least 75% of 60 images indicated a clear separation on the basis of protein expression between 6 and 12 week old animals and between the 3 experimental groups. Proteomic profiling revealed a significant up-regulation of mitochondrial enzymes such as isocitrate dehydrogenase, cytosolic malate dehydrogenase, and NADH dehydrogenase and significant down-regulation of signaling proteins such as 14-3-3 and structural proteins such as neurofilament light polypeptide (NEFL) in the perinatally asphyxiated group. Western blot confirmed the expression of isocitrate dehydrogenase was significantly up-regulated whereas, 14-3-3 zeta and NEFL were significantly down-regulated, in the asphyxia group across all age groups ($p<0.05$).

Conclusions: The differences elicited by perinatal asphyxia are consistent with emerging evidence for mitochondrial dysregulation in neurodevelopmental disorders, and may in time contribute novel biomarkers and fresh targets for prevention or treatment.

**171.009 9** Maternal Immune Activation during Pregnancy Induces Gender-Specific Behavioral Effects in Offspring. D. R. Hampson* and I. Xuan, *University of Toronto*

Background: Autism spectrum disorders are neurodevelopmental disorders that are characterized by two core symptoms; impaired social interactions and communication, and ritualistic or repetitive behaviors. Epidemiological and biochemical evidence suggests that a subpopulation of autism may be linked to immune perturbations that occur during fetal development. These findings have given rise to the maternal immune activation (MIA) model of neurodevelopmental disorders in which the offspring from female rodents who were subjected to an immune stimulus during early or mid-pregnancy are studied.

Objectives: The objectives were to (a) compare the induction of MIA using lipopolysaccharide (LPS) with that of polyinosinic:polycytidylic acid (Poly IC) in terms of behavioral effects on offspring, and (b) to examine gender effects of these treatments.

Methods: C57BL/6 mouse dams were treated with either LPS or Poly IC during mid-gestation to mimic a bacterial or viral infection respectively. Autism-associated behaviors were assessed in the adult offspring using motor activity tests to evaluate locomotion and exploration in a novel environment, two versions of the three-chamber

testing paradigm to test sociability, and the marble burying test and self-grooming analyses to investigate repetitive behavior.

Results: We found that prenatal LPS treatment caused female-specific increases in thigmotaxis behavior as well as modest decreases in sociability and self-grooming during habituation. In contrast, Poly IC treatment caused a male-specific reduction in motor activity concomitant with increased repetitive behaviors.

Conclusions: We conclude that autism-related behaviors observed in the mouse model of maternal immune activation are dependent on the type of immune stimulus given to the mother, and the gender of the offspring.

**171.010 10** Transcriptome Profiling in Engrailed2 Knockout Mice Reveals Common Molecular Pathways Associated with Autism Spectrum Disorders. P. Sgadò*, G. Provenzano, E. Dassi, V. Adami, G. Zunino, S. Genovesi, S. Casarosa and Y. Bozzi, *Centre for Integrative Biology (CIBIO), University of Trento, Italy*

Background: Transcriptome analysis has been used in autism spectrum disorder (ASD) to unravel common pathogenic pathways based on the assumption that distinct rare genetic variants or epigenetic modifications affect common biological pathways dysregulated in ASD.

Objectives: To unravel recurrent ASD-related neuropathological mechanisms, we took advantage of the *En2*$^{-/-}$ mouse model and performed transcriptome profiling on cerebellar and hippocampal adult tissues.

Methods: *En2*$^{-/-}$ and WT cerebellar and hippocampal tissue samples from three littermate mice were assessed for differential gene expression using microarray hybridization followed by RankProd analysis. To identify functional categories overrepresented in the differentially expressed genes we used integrated gene-network analysis, gene ontology enrichment and mouse phenotype ontology analysis. Furthermore, we performed direct enrichment analysis of ASD associated genes from the SFARI repository in our differentially expressed genes.

Results: Given the limited number of animals used in the study we used permissive criteria and identified 842 differentially expressed genes in *En2*$^{-/-}$ cerebellum and 862 in the *En2*$^{-/-}$ hippocampus. Our functional analysis revealed that the molecular signature of *En2*$^{-/-}$ cerebellum and hippocampus shares convergent pathological pathways with ASD, including abnormal synaptic transmission, altered developmental processes and increased immune response. Furthermore, when directly compared to the repository of the SFARI database, our differentially expressed genes in the hippocampus show enrichment of ASD-associated genes significantly higher than previously reported. qPCR was used with representative genes to confirm relative transcript levels compared to those detected in microarrays.

Conclusions: Despite the limited number of animals used in the study our bioinformatic analysis indicates the *En2*$^{-/-}$ mouse as a valuable tool to investigate molecular alterations related to ASD.

**171.011 11** Intrinsic Excitability Defects in Specific Subtypes of Medial Prefrontal Cortex Pyramidal Neurons in a Mouse Model of Autism. A. C. Brumback* and V. S. Sohal, *University of California, San Francisco*

Background: Autism, like many neuropsychiatric disorders, involves abnormal electrical activity in the brain. A leading hypothesis is that this abnormal activity results from an imbalance between neuronal excitation and inhibition. One main hypothesis for the proposed imbalance is that there is long-range underconnectivity but local hyperconnectivity in cortical microcircuits. Many of the major output neurons of cortex are located in Layer 5 (L5), and our lab recently showed that L5 of medial prefrontal cortex (mPFC) contains at least two distinct subpopulations of pyramidal neurons: "Type A" cells project subcortically, have prominent hyperpolarization-activated currents (Ih), thick-tufted apical dendrites, and express dopamine D2 receptors, whereas "Type B" neurons project to the contralateral cortex, have small Ih currents, thin-tufted apical dendrites, and lack D2 receptors.

Objectives: We hypothesize that in autism, the proposed pathological changes do not come about via global changes in the overall level of cortical excitation or inhibition, but rather reflect an imbalance of activity between these two subtypes of cortical pyramidal neurons.

Methods: We performed whole cell current clamp recordings from mPFC L5 Type A and B cells in acute brain slices from adult mice exposed to

valproate or saline in utero at embryonic day 10.5.

Results: We found that in the prenatal valproate exposure mouse model of autism ("VPA mice"), there is a defect in action potential generation in the cortically projecting (Type B) mPFC neurons but not the subcortically projecting (Type A) cells. In addition, we found that in VPA mice, Type A but not Type B cells had decreased frequency of action potentials to injected current. By elucidating how these subtype-specific cellular alterations relate to synaptic, EEG, and behavioral abnormalities, our studies may lead to new ways of understanding neuronal circuit dysfunction in autism.

Conclusions: By elucidating how these subtype-specific cellular alterations relate to synaptic, EEG, and behavioral abnormalities, our studies may lead to new ways of understanding neuronal circuit dysfunction in autism.

**171.012 12** Maternal Immune Activation Leads to Activated Inflammatory Macrophages in Offspring. C. E. Onore[1], J. Schwartzer[2], M. Careaga[3], R. F. Berman[4] and P. Ashwood*[5], (1)*MIND Institute, UC Davis*, (2)*The M.I.N.D. Institutue*, (3)*UC Davis/MIND Institute*, (4)*UC Davis*, (5)*University of California, Davis, MIND Institute*

Background: Several epidemiological studies have shown an association between infection or inflammation during pregnancy and increased risk of autism in the child. In addition, animal models have illustrated that maternal inflammation during gestation can cause autism-relevant behaviors in the offspring; so called maternal immune activation (MIA) models. More recently, changes in T cell cytokine responses were reported in children with autism and in offspring of MIA mice; however, the cytokine responses of other immune cell populations have not been thoroughly investigated in these MIA models.

Objectives: Similar to changes in T cell function, we hypothesized that following MIA, offspring will have long-term changes in macrophage function.

Methods: To test this theory, we utilized the polyinosinic-polycytidylic acid [poly(I:C)] MIA mouse model in C57BL/6J mice and examined macrophage cytokine production in adult offspring. Pregnant dams were given either a single injection of 20 mg/kg poly(I:C), or saline delivered intraperitoneally on gestational day 12.5. When offspring of poly (I:C) treated dams reached 10 weeks of age, femurs were collected and bone marrow-derived macrophages were generated. Cytokine production was measured in bone marrow-derived macrophages incubated for 24 hours in either growth media alone, LPS, IL-4/ LPS, or IFN-γ/ LPS.

Results: Following stimulation with LPS alone, or the combination of IFN-γ/LPS, macrophages from offspring of poly (I:C) treated dams produced higher levels of IL-12(p40) ($p < 0.04$) suggesting an increased M1 polarization. In addition, even without the presence of a polarizing cytokine or LPS stimulus, macrophages from offspring of poly (I:C) treated dams exhibited a higher production of CCL3 ($p = 0.05$). Moreover, CCL3 levels were further increased when stimulated with LPS, or polarized with either IL-4/LPS or IFN-γ/LPS ($p < 0.05$) suggesting a general increase in production of this chemokine.

Conclusions: Collectively, these data suggest that MIA can produce lasting changes in macrophage function that are sustained into adulthood.

**171.013 13** Mother Recognition and Preference after Neonatal Amygdala Lesions in Rhesus Macaques (Macaca mulatta) Raised in a Semi-Naturalistic Environment. A. P. Goursaud*[1], K. Wallen[2] and J. Bachevalier[1], (1)*Yerkes National Primate Research Center, Emory University*, (2)*Emory University*

**Background:**

Attachment to the caregiver, typically the biological mother, is crucial to young mammals' socio-emotional and cognitive development and its disruption leads to long-term negative outcomes. Although studies in nonprimate species suggest that the amygdala regulates social preference and attachment development, its role in primate filial attachment development has been little investigated and has produced mixed results. In addition, in none of the earlier studies conducted in nonhuman primates (rhesus monkeys) did the mother-infant pairs live in large social environment characteristic of rhesus monkey societies.

**Objectives:**

This study aimed to assess the specific contribution of the amygdala in the development of filial attachment in primates. We specifically explored the effects of selective bilateral neonatal

lesions of the amygdala or sham-operation on the expression of a preference for the biological mother, as well as proximity and comfort-seeking behaviors toward the mother, as compared to another familiar adult female, in infant monkeys raised in a species-typical social environment.

**Methods:**

Twenty-eight male and female infant rhesus macaques (*Macaca mulatta*) reared by their mother in complex social groups of about 100 animals underwent selective bilateral lesion of the amygdala (Neo-A, N = 16) or sham-operation (Neo-C, N = 12) at 2-3 weeks of age. Animals were given a preference test (mother vs. familiar female) at 3 and 6 months of age in an experimental, but familiar, environment allowing manual contact with the stimuli.

**Results:**

Neonatal amygdalectomy did not affect social discriminative abilities and mother preference at 3- and 6-month-old. Nevertheless, as compared to sham-operated controls, amygdalectomized infants were less often in physical contact with their mother across the two testing ages, sought less often proximity with their mother at 3 months as well as reached less often for their mother while in proximity at 6 months.

**Conclusions:**

These data strongly suggest that the amygdala is not involved in the cognitive processes underlying recognition of and preference for the mother in primates. However, there is still the possibility of an involvement of the amygdala during the formation of the mother-infant bond during the first few postnatal weeks. The findings also indicate that the amygdala might be critical in the development of higher cognitive processes necessary for the maintenance of social relationships and/or the establishment of new ones later on, since the amygdalectomized animals displayed less physical contacts with their mothers. The findings are discussed in relation to the known contribution of the amygdala to filial attachment in both rodents and humans.

**171.014 14** Relative Lack of Volumetric Differences in the Brain of Mouse Models Involving the Serotonin Transporter Gene. J. Ellegood*[1], C. L. Muller[2], T. M. Kerr[2], R. D. Blakely[2], R. M. Henkelman[3], J. Veenstra-Vander Weele[2] and J. P. Lerch[3],

(1)*Hospital for Sick Children*, (2)*Vanderbilt University*, (3)*University of Toronto*

Background: Serotonin (5-HT) is a neurotransmitter that plays a key role in brain development (Sodhi and Sanders-Bush, 2004). Further, the 5-HT transporter gene (SLC6A4, SERT) has been associated with both 5-HT levels and autism susceptibility.

Objectives: The purpose of this work was to assess the volumetric differences in the brains of three different SERT mouse models and corresponding wildtype littermates using MRI.

Methods: In total, 120 fixed mouse brains were examined from three different SERT mouse models. The first group was a SERT KO model, and the other two groups were SERT Ala56 KI models on two different backgrounds (129S6/S4 and C57BL/6). Each group consisted of 40 mice, 20 wildtype littermates (WT) and 20 SERT mice (Age = P60, 10 Male and 10 Female).

*MRI Acquisition* – Scan parameters: T2- weighted, 3D fast spin-echo sequence (TR - 2000 ms, TEs - 14 ms, 6 echoes, 2 averages, FOV - 14 x 14 x 25 $mm^3$, Matrix size = 250 x 250 x 450). This sequence yielded an image with 0.056 mm isotropic voxels (3D pixel). Total imaging time ~12 h (Lerch et al., 2011).

*Data Analysis*– To visualize and compare any differences, the images from each of the three groups are registered together. The goal of the registration is to model how the deformation fields relate to genotype (Lerch et al., 2008). Volume differences can then be calculated for 62 regions in each groups (Dorr et al., 2008). Multiple comparisons were controlled for using the False Discovery Rate (FDR) (Genovese et al., 2002).

Results: No significant volume differences were found in the brains of either SERT Ala56 KI models, measured in both absolute ($mm^3$) and relative (% total brain) volume. Minimal differences were found in the SERT KO model, and these differences were driven solely by the female mice. Several volume differences in the female SERT KO mice were found with absolute volume, but only two regions, the cerebral peduncle and lateral septum, were found to be significantly different with relative volume in the female SERT KO mice.

Conclusions: It has been shown previously that behavioural phenotypes are associated with neuroanatomical phenotypes in 87% of models (Nieman et al., 2007). Furthermore, in the 30+ autism models we have currently examined >75% of the models have neuroanatomical phenotypes. Therefore, these results are quite interesting, as both the SERT KO and Ala56 KI models have known behavioural and physiological phenotypes; although the phenotype of the SERT KI on the B6 is different from the 129S6/S4 (Moy et al., 2009; Kalueff et al., 2010; Veenstra-VanderWeele et al., 2012; Kerr et al., 2013). These null findings may indicate that developmental effects of altered extracellular 5-HT levels do not result in structural brain changes at a mesoscopic scale; although they do not rule out finer grained changes in connectivity or neuronal migration. Effects of sex and sex hormones are important to consider in future studies of serotonin's role in brain development and function.

**171.015 15** Serotonin 1A Agonism Selectively Inhibits Affiliation in the Titi Monkey: Relevance to Social Deficits and Hyperserotonemia in Autism. R. H. Larke* and K. L. Bales, *University of California, Davis*

Background: Hyperserotonemia is present in roughly one third of individuals with autism, and central deficits in serotonin and oxytocin are associated with autism. Early in life, serotonin in blood may be activating 1A autoreceptors in the brainstem involved in a negative feedback loop which decreases serotonin activity in higher brain areas. Rodent models of hyperserotonemia indicate that it leads to an autistic-like phenotype, yet the processes involved in the suppression of social behavior in this model remain unclear, and comparative work in non-human primates is needed.

Objectives: To model the effects of activation of the serotonin 1A negative feedback loop on affiliative behavior in male pair-bonded titi monkeys, in order to examine how serotonin autoreceptor activity is involved in social behavior. We also sought to characterize changes in peripheral oxytocin, vasopressin, and cortisol due to serotonin 1A agonism, and to correlate these peripheral measures with social behaviors of interest.

Methods: 8 adult male titi monkeys in established pair bonds were administered 0.1 mg/kg 8-hydroxy-2-(di-n-propylamino)-tetralin (8-OH-DPAT, a selective serotonin 1A receptor agonist) or saline vehicle daily for 15 consecutive days. Blood samples were taken 15 and 45 minutes post injection on days 1, 3, 8, 10 and 15. Behavior was recorded daily for 30 minutes with the pair-mate and coded for locomotor, sexual, arousal and affiliative behaviors. Blood plasma was assayed for oxytocin, vasopressin and cortisol.

Results: 8-OH-DPAT significantly inhibited affiliative behavior, including reductions in approaching the pair mate ($F_{1,209}$ = 18.42, $p$<.0001 ), initiation of physical contact ($F_{1,208}$ =14.54 , $p$<.001), duration of passive contact ($F_{1,209}$ = 4.85, $p$<.05), and lipsmacking ($F_{1,211}$ = 72.64, $p$<.0001). Oxytocin was significantly increased relative to the saline group ($F_{1,61}$ =4.71, $p$<.05) and a significant time by treatment interaction was found for cortisol ($F_{1,64}$= 5.6, $p$<.05).

Conclusions: Excess serotonergic autoreceptor activity decreases affiliative behavior in male titi monkeys, indicating that this process can directly impact social behavior absent a developmental context. Serotonin 1A autoreceptor agonism resulting from hyperserotonemia may be a significant factor leading to the social deficits seen in autism.

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**171.016 16** Social Choice in the BTBR Mouse Model of ASD. K. K. Chadman*[1], K. Ryan[2] and L. Thompson[2], (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*CUNY College of Staten Island*

Background: The social approach test examines sociability in mice that have a choice between interacting with a stranger mouse or a novel object. Most mice spend more time with the stranger mouse which is interpreted as normal sociability, for example the C57BL/6J (B6) mice. The BTBR T+*tj*/J (BTBR) strain of mice do not spend more time with the stranger mouse, which appears to be independent of partner strain (Yang et al. 2012 Physiol & Behavior 107:649). There is evidence that olfactory cues are sufficient to provide a social cue in this test in the B6 mice (Ryan et al. 2008 Beh Brain Res 193:235). It is unclear if the BTBR mice will prefer to spend time with more social (B6) mice or the less social

(BTBR) mice or what aspects of the stranger mice determine preference in the BTBR mice.

Objectives: To test the social preference of these different strains of mice, the subject mouse given a choice between two stranger mice, one with "normal" (see above) sociability or one with lower sociability (BTBR). The preference of the subject mouse for a stranger mouse or dirty bedding from the stranger mouse cage was also tested.

Methods: The three chambered social approach apparatus was used very similarly to previous studies. The modifications were during the sociability phase. For the first experiment, there was a mouse placed in each side chamber – a B6 on one side and a BTBR mouse on the other counterbalanced across subject mice. For the second experiment, each side chamber contained either a stranger mouse or bedding from the stranger mouse cage, counterbalanced across subject mice. All stranger mice were the same sex as the subject mice.

Results: The B6 mice did not show a preference for any partner strain while the BTBR mice preferred the B6 mice. Results from the bedding experiment were more complex with males and females having different profiles. Male B6 mice did not show a preference between the stranger mouse and bedding, while the male BTBR preferred the bedding regardless of stranger mouse strain. Female B6 and BTBR mice preferred bedding when the stranger strain was different, no preference was observed with the stranger strain was the same.

Conclusions: BTBR mice have low sociability in general, prefer to spend time with the more social B6 mice when given a choice. This suggests that there is a perceptible difference between the strains that guides the choice of the BTBR mice into preferring the more social stranger mice. In the choice between bedding and a stranger mouse, behavior of the female mice was dependent on the stranger mouse strain (same or different from subject mouse strain). The male mice had a different pattern, the B6 mice investigated both the stranger mouse and stranger mouse bedding similarly regardless of the strain of the stranger mouse. Male BTBR mice spent more time with the bedding which may indicate some social anxiety associated with the awake moving stranger versus the similarly smelling bedding.

**171.017 17** mGluR5 Expression Is Required for NMDA-Receptor Dependent Forms of Plasticity in Mouse Visual Cortex. M. Sidorov*[1], E. Kaplan[1], S. Tagliatela[1] and M. F. Bear[2], (1)*Massachusetts Institute of Technology*, (2)*The Picower Institute for Learning and Memory*

Background: Fragile X (FX) is a single-gene disorder associated with autism. Fragile X is caused by a mutation in the *Fmr1* gene, leading to a lack of production of its protein product, Fragile X mental retardation protein (FMRP). FMRP normally acts as an inhibitor of protein synthesis at the synapse, and the lack of FMRP leads to increased protein synthesis. Fragile X is essentially thought of as a disease of excess – excessive protein synthesis causes numerous symptoms, and interventions designed to reduce protein synthesis back to normal levels are being considered as possible therapies. Metabotropic glutamate receptors (mGluR) signaling is coupled to synaptic protein synthesis. Therefore inhibiting this pathway could potentially rescue the enhanced protein synthesis seen in Fragile X. The "mGluR theory of Fragile X" has been extensively tested. Most recently, chronic administration of the novel mGluR5 antagonist CTEP corrected numerous FX mouse phenotypes.

Objectives: We sought to understand how mGluR5 regulates experience-dependent synaptic plasticity in mouse visual cortex. This is critically important because mGluR5 antagonists are currently in clinical trials for FX.

Methods: We measured synaptic plasticity in vitro using both whole-cell and field potential recordings, and in vivo in an awake, head-fixed setup where the animal views visual stimuli.

Results: Surprisingly, we found that mGluR5 is required for long-term depression (LTD) in slice and forms of experience-dependent plasticity in vivo. Additionally, chronic administration of the mGluR5 antagonist CTEP results in similar phenotypes seen in the mGluR5 knockout mouse.

Conclusions: This work suggests that signaling through mGluR5 during development is crucial to establish forms of NMDA receptor-dependent plasticity in adulthood. In the context of Fragile X, this work suggests that the timing and location

of mGluR5-mediated pharmacological therapies are crucial.

## 172 Cognition: Attention, Learning, Memory

**172.019 19** "Catch the Spies": Multiple-Object Tracking in Low-Functioning Children with Autism Spectrum Disorder. H. Flores*[1], D. A. Brodeur[2], L. M. Trick[3] and J. A. Burack[1], (1)*McGill University*, (2)*Acadia University*, (3)*University of Guelph*

Background:

The multiple object tracking (MOT) task, considered an index of dynamic information processing as it involves the ability to focus on and track target objects as they move among distracters, allows us to better understand the real-world attentional task of focusing on dynamic objects or events in complex, busy environments. This ecologically relevant task requires individuating several items at once and assigning mental reference indexes to a small number of selected targets so that the locations of the targets can be reported even if their properties and positions change (Pylyshyn, 2001). Since cognitive resources must be simultaneously assigned to multiple, moving objects for successful task completion, MOT is considered a measure of object-based visual attention with real-world applicability (Scholl, 2009). The preference for local processing (Happe & Frith, 2006) and strengths in visual search (Plaisted et al., 1998) among persons with ASD suggest that their performance on the MOT task might be enhanced relative to developmental level.

Objectives:

To examine dynamic attention abilities in individuals with ASD, with the administration of an MOT task to children with ASD as compared to that of TD children matched on mental age (MA).

Methods:

Groups of low-functioning children with ASD ($n$ = 11) and TD children ($n$ =10) were matched at a developmental level of 7 years of age on visual-spatial abilities as measured by the Leiter-R International Performance Scale Revised (Roid & Miller, 1997). As a measure of MOT, we administered Catch the Spies Task (Trick et al., 2005; 2009), a computer game in which the participants were asked to keep track of the locations of 1-4 spies (targets) that were disguised to look like other people (happy-face figures) in a display. Both the targets and the distracters moved randomly and independently throughout each trial for 4 seconds. To ensure that any MOT effects did not originate from differences in encoding or reporting the target positions or remembering the target positions after a delay, control tasks requiring the reporting of target positions for static items immediately after the presentation of or 4 seconds following the presentation of targets were administered.

Results:

The children with ASD showed similar performance to their MA-matched typically developing peers in their ability to track one through four targets on the MOT task (all p-values > .50). Both the ASD and the TD group were able to track two items reliably but were unable to track four items [Means (SE) for ASD: 1 target = 76(10), 2 targets = 73(8), 3 targets = 70(7), 4 targets = 59(6); and, TD: 1 target = 84(5), 2 targets = 79(6), 3 targets = 68(5), 4 targets = 55(4)]. The groups also performed similarly on immediate and delayed report tasks.

Conclusions:

Low functioning children with ASD performed similarly to the MA-matched TD group in that they were able to track up to 2 items but unable to track 4 items. The findings suggest typical development in ASD individuals of processes required for MOT including object individuation and dynamic tracking.

**172.020 20** A Preliminary Head-Mounted Eye-Tracking Study of Individuals with ASD Touring a Museum of Art. S. J. Wallace*[1], G. Vaccarino Gearty[2], E. S. Kim[1], M. Perlmutter[1], Q. Wang[1], C. A. Wall[1], J. S. Kowitt[3], L. Friedlaender[4] and F. Shic[1], (1)*Yale University School of Medicine*, (2)*University of Chicago*, (3)*University of Connecticut*, (4)*Yale University*

**Background:** Eye tracking is a powerful tool for studying attention patterns, revealing differences in attention to people's mouths, eyes, and activities among individuals with typical development (TD) and autism spectrum disorders (ASD). Many current eye tracking studies have used table-mounted devices to examine pre-recorded video stimuli. However, commercial head-mounted eye trackers can be expensive, limiting accessibility. Gaze tracking in real world situations may offer insight into the difficulties

individuals with ASD experience in authentic social interactions.

**Objectives:** 1) To construct an untethered head-mounted eye-tracking device; 2) To contrast patterns of attention in individuals with ASD and TD towards people in paintings and social situations.

**Methods :** We used inexpensive electronic components to construct untethered head-mounted eye trackers. A tour guide escorted pairs of participants ($n$ = 9, ASD; $n$ = 13, TD) through an art museum to view four paintings featuring a variety of social content. For each painting, participants completed three tasks: (1) silently observing the painting, (2) listening while the guide spoke, and (3) answering open-ended and rating questions asked by the guide (*QA*) . Behavioral coding was completed on all participants. Eye-tracking data has been analyzed for ($n$ = 5, ASD; $n$ = 3, TD). To track gaze, we detected the pupil centroid and estimated a map from its position to calibration targets in scene videos.

**Results:** Linear mixed model analyses revealed a task x group interaction for within-painting regions of interest ($p$ < .01). During the QA task, participants with ASD looked more at the painting background than did TD individuals ($p$ < .05). This effect was absent in the silent observation task, and marginally significant ($p$ = .080) during the listening task. While looking at the guide or the other participant, participants with ASD looked less at people's eyes than did TD participants ($p$ < .05). There also was a task x group interaction for duration spent looking at real world versus the paintings ($p$ < .05), with ASD and TD participants showing opposite patterns of attentional allocation. Behavioral coding showed a higher number of shifts of attention to the guide ($p$ < .05) and to the painting ($p$ < .05) by participants with ASD than by TD participants. Participants with ASD gestured more than TD participants ($p$ < .05).

**Conclusions:** High-functioning adults with ASD show similar gaze patterns towards paintings as do TD adults during silent viewing. These patterns become more atypical as the social demands imposed by the guide increase. During real-world social interactions, individuals with ASD showed decreased attention towards the eyes of others. Individuals with ASD tended to monitor the real world more than typical individuals, and engaged in more discrete shifts of attention during social interaction, suggesting either executive function or social information processing deficits. More prototypical patterns of attention towards paintings in the absence of communicative processing demands may be due to an equalizing effect of art on attention, or the static nature of the painting compared with the dynamic, social nature of interaction with the guide.

**172.021 21** A Systematic Examination of Early Perceptual Influences on Low-, Mid- and Higher-Level Visual Abilities in Autism Spectrum Disorder. J. Guy*[1], A. Perreault[1], V. M. Doobay[2], L. Mottron[3] and A. Bertone[4], (1)*Perceptual Neuroscience Laboratory for Autism and Development (PNLab)*, (2)*McGill University*, (3)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (4)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

**Background:** It is now well accepted that perceptual alterations are a key characteristic of the autistic behavioral phenotype (Mottron 2006, Bertone et al 2010a). Studies investigating visual perception in Autism Spectrum Disorder (ASD) have identified atypical abilities mediated by low- (primary visual areas), mid- (extra-striate areas) and higher-levels (large-scale neural functioning) of processing. The bulk of this research, however, has focused on individual levels of processing in isolation (i.e. low or high). It is therefore unknown if a functional relationship exists between levels of information processing in ASD, and more so, if alterations in early levels of visual analysis influence mid- and higher-level perception. The answer to this question is critical in understanding the origins of the autistic perceptual phenotype and ultimately, the effect of early encoding on subsequent perceptual, cognitive and social abilities.

**Objectives:** The goal of this set of studies was to systematically assess whether manipulating either (i) the type (luminance vs texture), or (ii) access to early, local information differentially affects autistic performance on tasks targeting low-level (spatial frequency perception), mid-level (global form perception) and higher-level (visuo-spatial and face identity perception) perceptual processes.

**Methods:** Four separate studies examining the effect of manipulating physical stimulus properties

on progressively complex visuo-spatial tasks were conducted: (i) low-level perception was assessed using vertically oriented, sine-wave luminance- and texture-defined gratings over a range of low to high spatial frequencies; (ii) mid-level perception was examined using luminance and texture-defined radial-frequency patterns (RFPs): closed-contour spatial stimuli manipulated to create "bumps" or radial frequencies along their quasi-circular contours to optimize global (i.e. few bumps) and local (i.e. many bumps) processing; (iii) higher-level, non-social perception was assessed using a reversed block design task where the physical attributes of the block stimuli were manipulated (luminance vs texture); (iv) higher-level, social perception was assessed with a face-identification task incorporating four view conditions (front-view, side-view, inverted and view-change conditions) where access to local and global cues was manipulated.

**Results:** For the low-level task, results revealed an increased sensitivity of the ASD group for high-spatial frequency information for the luminance-defined condition alone. For the mid-level task, individuals with ASD were significantly worse at discriminating texture-defined RFPs across all modulation conditions. However, the ASD group performed as well as the control group for the luminance-defined RFPs with many modulations along their contour: a condition that biases local information processing. For the higher-level, non-social block design task, individuals with ASD outperformed the control group when blocks were luminance-defined; however, this "cognitive peak" disappeared when blocks were texture-defined. For the higher-level, social task, individuals with ASD were significantly worse in identifying faces in the view-change condition only, which limited local information cues.

**Conclusions:** Our findings indicate that visual abilities mediated by low-, mid- and higher-level mechanisms in autism are differentially affected by the nature and access to early visual information during task completion. These results provide compelling evidence to suggest that early perceptual alterations in autism are at least in part responsible for autism's perceptual phenotype, irrespective of the level at which it is defined.

**172.022 22** Arbitrary Cue-Target Association on a Visual Orienting Task Is Enhanced in Individuals with Higher Autism Quotient Scores. O. Landry*[1] and I. L. Kehayes[2], (1)*McMaster University*, (2)*Dalhousie University*

Background: The Broader Autism Phenotype (BAP) refers to a subclinical presentation of behaviours, preferences, and cognitive style that resembles autism. There are a growing number of studies that find that certain cognitive profiles vary as a function of the BAP, particularly visual attention. Visual attention is typically measured using a Posner task, where attention is cued using a simple cued target detection task. When cues are congruent with the target location, reaction times are faster than when cues are incongruent. Peripheral cues (i.e., a brief flash) elicit an involuntary orienting response, whereas central arrow cues direct attention away from the arrow to the location indicated by the arrow. Past research has found that individuals with autism show a typical response to peripheral cues, but an impaired response to central arrow cues. Previous research examining visual orienting in the BAP suggests similar patters, but research is limited.

Objectives: To examine performance on visual orienting as a function of the BAP using a central arrow cue (i.e., the direction condition), peripheral cue, and an arbitrary cue. The arbitrary cue was not explained to participants and thus in order to demonstrate an orienting effect, participants would have to learn the cue's meaning over the course of the experiment.

Methods: Thirty university undergraduate students completed the Autism Quotient questionnaire, which measured their autistic-like traits, and a Posner-type visual orienting task under the three cuing conditions: peripheral, directional (central arrow), and arbitrary colour cues.

Results: Overall, participants demonstrated orienting on all three conditions. Autism Quotient scores ranged from 5 to 37, and were correlated with orienting magnitude on the arbitrary condition only ($r > 0.4$). The correlation was positive, indicating that higher Autism Quotient scores were associated with larger orienting effects on this condition, and thus enhanced efficiency at learning this novel cue-target association.

Conclusions: The positive association of high AQ and enhanced efficient at learning the arbitrary cue contingency suggests a potential enhancement of visually-based associative learning in high AQ individuals. Future studies will need to explore the potential advantage of having a higher AQ without clinically significant impairment. Mapping the cognitive profile associated with the BAP may provide clues to the causes and underlying mechanisms that are associated with the impairments found in individuals with autism.

**172.023 23** Associations Between Sensory Response Patterns and Symptoms of ADHD in Children with ASD. E. Patten*, C. Cotton and E. Smith, *UNC Greensboro*

Background: Although the DSM-5 allows for dual diagnosis of ASD and ADHD, debate continues regarding the validity of comorbidity with estimates spanning 14-78% (Gargaro, et al., 2011). This sizable comorbidity range may suggest that symptoms of inattention and hyperactivity associated with ADHD are not consistently defined across studies or worse, suggest misinterpreted symptoms.

ADHD is the second most common co-occurring diagnosis with ASD (Simonoff et al., 2008) and if co-occurring diagnoses can be addressed early in development then overall outcomes in children with ASD may be improved. Although ADHD is most frequently addressed with stimulant medications in children who are otherwise typically developing, stimulant medications can result in negative side effects in some children with ASD. Thus, distinguishing attention symptoms that are intrinsic to ADHD versus attention symptoms that are features of ASD may be an important objective for early and appropriate diagnosis and intervention. We were interested in understanding the extent to which parent reported symptoms of ADHD are associated with unusual sensory processing.

Objectives: **(**1) To examine associations between symptoms of ADHD (Inattention and hyperactivity/impulsivity) and sensory response patterns (hyporesponsiveness, hyperresponsiveness, and sensory seeking) and (2) To examine associations between symptoms of ADHD and sensory responses to social and nonsocial sensory stimuli in children with ASD.

Methods: 15 preschool children with ASD (CA: M=58 months, SD=11; MA: M=36 months, SD=13) were assessed for symptoms of attention through the *ADHD Rating Scale IV-Home Version*, an 18-item parent questionnaire based on the DSM-IV criteria for ADHD diagnosis (DuPaul et al., 1998) that has been successfully used to assess symptoms of ADHD in preschool children (McGoey et al., 2007). The *Sensory Experiences Questionnaire, version 2.1* (SEQ 2.1; Baranek, 1999), a 42-item caregiver questionnaire was used to assess sensory responsiveness (hyporesponsiveness, hyperresponsiveness, sensory seeking) across modalities (e.g., visual, tactile, auditory).

Results: (1) *Inattention* was significantly associated with sensory hyperresponsiveness, $r(15) = .64$, $p = .01$, association with sensory hyporesponsiveness was nearly significant, $r(15) = .51$, $p = .06$. Inattention was not significantly associated with sensory seeking, $r(15) = .21$, $p = .46$. *Hyperactivity/Impulsivity* was significantly associated with sensory hyporesponsiveness, $r(15) = .58$, $p = .25$ and sensory hyperresponsiveness, $r(15) = .55$, $p = .022$, but not with sensory seeking, $p = .87$. (2) *Inattention* and *Hyperactivity/Impulsivity* were both associated with responsiveness to social stimuli, $r(15) = .71$, $p = .003$ and $r(15) = .65$, $p = .01$ but only *Inattention* was associated with nonsocial stimuli $r(15) = .54$, $p = .04$.

Conclusions: The findings of this study may suggest that parents could have difficulty distinguishing between attention symptoms characteristic of ASD versus ADHD. Alternatively, sensory response patterns may influence the development of attention. Additionally, both subcomponents of ADHD are significantly associated with social attention while only inattention was associated with nonsocial stimuli. Further research is needed to better understand the nature of the associations between symptoms of ADHD and sensory response patterns in ASD.

**172.024 24** Attention to Non-Social and Social Details in Adults with High and Low Degrees of Autistic Traits: A Change Blindness Study. C. Singleton*, M. J. Brosnan and C. Ashwin, *University of Bath*

**Background:**

Non-social behaviours, such as repetitive actions and restricted interests, form one of the

diagnostic criteria for Autism Spectrum Disorders (ASDs). The cognitive mechanisms underlying non-social processing and how they relate to social processing are not well understood. Researchers have suggested that these two cognitive features of ASD may be unrelated to each other in the typically developing population and that they may demand separate explanations. It is therefore suggested that research on these two processes in the neurotypical population should clarify their relatedness. Attention to detail is posited as one of the features of non-social processing seen in ASD. Methods for assessing attention to detail include Change Blindness tasks, which measure how quickly it takes to identify changes in a flickering visual scene.

**Objectives:**

The aim of this study was to establish whether attention to social and non-social aspects of a visual scene are related to each other and to degree of autistic traits, and therefore whether non-social and social behaviours such as those seen in ASD may in fact be explained together in terms of attentional biases.

**Methods:**

56 participants (28 male, 28 female) completed the Autism Quotient (AQ) questionnaire to measure ASD traits before completing a Change Blindness task designed to include 52 scenes including both social and non-social features, 26 images featuring social changes (e.g. changes to a person's face) and 26 featuring non-social changes (e.g. a change to a vehicle). Each initial image was interrupted with a blank screen for 500ms before the change image was shown. Each image 'flickered' until the participant spotted the change and pressed a key to record the time taken to spot it. An average response time was calculated for both the social and non-social changes. A bivariate correlation was then used to investigate the relationship between mean response time and AQ for each condition. A paired-samples t-test was employed to explore differences between response time to the social and non-social changes across the whole sample.

**Results:**

Analysis revealed a significant correlation between AQ and response time to social changes. There was no significant correlation between AQ and time taken to spot the non-social changes. There was a significant correlation between response time to social and non-social changes. The paired-samples t-test revealed significant differences in response time for social and non-social changes, participants taking significantly longer to identify the non-social changes.

**Conclusions:**

AQ is related to greater difficulty identifying social changes, implying that those with more autistic traits pay less immediate attention to social details. Overall, people took longer to identify non-social changes, implying that in a neurotypical population social details are attended to immediately. The strong correlation between response time to social and non-social changes indicates that, at an attentional level at least, these two cognitive features of ASD may not be wholly independent of one another.

**172.025 25** Can Reasoning and Decision Making in ASD be Conceptualised As More Deliberative or Less Intuitive?. M. Brosnan*[1], M. E. Hollinworth[1] and K. Antoniadou[2], (1)*University of Bath*, (2)*Maastricht University*

Background: Dual-process accounts of human cognition suggest two distinct types of reasoning and decision-making; a fast 'intuition' that is independent of working memory and cognitive ability and a slower analytical-logical 'deliberation' that is heavily dependent on working memory and related to individual differences in cognitive ability. Those with Autism Spectrum Disorder (ASD) can tend towards deliberative reasoning and decision-making which some authors have attributed to impairment within the rapid/ intuitive mechanisms. However, intuition has not been explicitly assessed in ASD. The Cognitive Reflection Test (CRT) is a three-item assessment designed to measure the tendency to override a prepotent intuitive response that is incorrect and to engage in further deliberation that leads to the correct response. As the CRT is a performance measure that can provide indication of intuitive responses and deliberative responses (as well as erroneous responses), it has been widely used within the general population. Sex differences have been identified that suggest females are more intuitive and males are more deliberative. The Extreme Male Brain (EMB) theory of autism proposes that sex differences in the general population are exaggerated within ASD.

Objectives: Identify whether those with ASD will be both more deliberative and less intuitive.

Methods: Participants comprised of 21 people with a clinical diagnosis of ASD (4 female), and 21 males and 38 females (mean age 20 years, sd=2.5). Participants were taken from the University population and the ASD participants additionally self-completed the Ritvo Autism Asperger Diagnostic Scale-Revised and a significant other (typically a parent) completed the Social Communication Questionnaire. All participants undertook a computer-based version of the CRT. This allowed for the order of questions to be randomised and response times to be recorded.

Results: ANOVA analyses revealed a group difference in Deliberative responses (ASD(1.9) > male(1.3) > female(0.8): $p<.001$) and Intuitive responses (ASD(0.9) < male(1.2) < female(1.7); $p<.05$). There were no significant group differences in incorrect responses or time taken to complete the test, or time to make either deliberative or intuitive responses (all $p>.05$). Post-test analyses revealed that for Deliberative responses the ASD group scored significantly higher than the male group who in turn scored significantly higher than the female group ($p<.05$). For Intuitive responses, the ASD group significantly lower than the female group ($p<.001$; neither group differed significantly from the male group).

Conclusions: The results are consistent with conceptualising ASD as a relatively more deliberative reasoning and decision making style. Although there was a trend for ASD to be associated with less intuitive reasoning and decision making, the ASD group did not differ from the male group. The results are consistent with the EMB theory of Autism and suggest dual cognition accounts are relevant to understanding ASD. The timing data suggest that a speed-accuracy trade-off account cannot fully explain the findings. The ASD group responded in a manner suggesting that prepotent intuitive responses were being overridden and further deliberations were being undertaken. This, however, does not necessarily imply impairment within rapid/intuitive mechanisms.

**172.026 26** Can Sequential Processing be Enhanced As a Way to Improve Language and Communication Functions?. G. L. Smith*, C. M. Conway and J. C. Daltrozzo, *Georgia State University*

Background: One of the core symptoms of Autism Spectrum Disorder (ASD) is "persistent deficits in social communication and social interaction across multiple contexts," and can include an impairment to language (5th ed.; *Diagnostic and Statistical Manual of Mental Disorders*; American Psychiatric Association, 2013). Rather than relying on standard therapeutic approaches that focus on behavioral outcomes, it may be beneficial to develop interventions that attempt to modify the underlying neurocognitive mechanisms that are the basis for the language and communication symptoms observed in ASD. One possible explanation for the observed pattern of deficits in language and communication functions is that ASD is associated with impaired "sequential processing" abilities. Sequential processing (SP) is a domain-general mechanism used to perceive and learn environmental patterns of stimuli unfolding in time, especially in the domains of language, social, and motor cognition (Cleeremans et al., 1998; Conway et al., 2010). Both high-functioning and lower-functioning children with ASD have been shown to be impaired on sequential processing tasks (Gordon & Stark, 2007; Maister & Plaisted-Grant, 2011; Mostofsky et al., 2000). Thus, because of the established link between SP and language in typically-developing (TD) children and adults (Conway et al., 2010) and the evidence suggesting an impairment of various aspects of SP in ASD, it is possible that impairments to SP are a contributing factor to the observed difficulties in language and communication.

Objectives: Under this view, a potentially promising treatment approach is to enhance SP in order to improve language and communication skills in individuals with autism.

Methods: In order to test the feasibility of this approach we developed a novel computerized training task to attempt to enhance SP in healthy TD adults. Participants (n=24) were quasi-randomly assigned to a SP training group, active control group, or passive control group. The SP training involved a computerized visual-spatial sequence reproduction task that incorporated underlying structured patterns in the input sequences. We used event-related potentials

(ERP) to explore the neural changes to SP and language resulting from the sequence training. Participants were first assessed on several baseline behavioral and ERP measures of SP and language and then following 10 days of training or control tasks, participants were reassessed with the same baseline measures.

Results: Results indicated training-related behavioral enhancements to SP and language. In addition, sequence training led to a frontal functional neural reorganization of SP, a region of the brain known to be important for executive functions, controlled attention, and language.

Conclusions: Overall, these findings demonstrate the feasibility of using this intervention to alleviate the most central deficits of autism. Specifically, a targeted intervention strategy that focuses on training underlying SP mechanisms could provide benefits to the quality of life for individuals with ASD by improving their ability to acquire the subtle patterns embedded in language, and possibly other domains where such learning is important, such as pragmatics and social interactions.

**172.027 27** Cognitive Control and Negative Affect: A Dimensional Approach to Self-Regulation in Autism and Other Childhood Psychopathologies and Developmental Disorders. B. Yerys*[1], R. T. Schultz[2], L. D. Antezana[3] and J. Herrington[2], (1)*The Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*, (3)*Children's Hospital of Philadelphia*

Background:

Self-regulation enables individuals to make decisions, control impulses or thoughts, and to engage in pro-social behavior. Impaired self-regulation contributes to pervasive impairments and poor outcomes in a variety of childhood disorders, including children with autism spectrum disorders (ASD). A number of studies have examined cognitive control and affective processes independently within a single pediatric population; however recent models suggests that the dynamic interplay of cognitive control and affective processes is critical to understanding self-regulation failures. Approaching the problem in terms of a dynamic interplay also easily allows study of affect regulation across populations, a movement in current research spurred by the NIMH's Research Domain Criteria (RDoC) framework on mechanisms operating as dimensions of function from typical to atypical childhood outcomes.

Objectives:

The current study aims to test the model by assessing whether the linear relationship between negative affect and self-regulation impairments is mediated by cognitive control.

Methods:

282 children were enrolled in the present study; 167 had an ASD, 27 had an anxiety disorder, 24 children enrolled in the study with concerns about an ASD but did not meet criteria, and 64 typically developing controls. This group ranged in age from 6.0 to 15.3 years ($M$=9.88 years, SD=2.74) with general cognitive ability ranging from 30-155 ($M$=98.65, SD=22.70). The Externalizing and Internalizing subscales from the Behaviors Assessment Scale for Children-2$^{nd}$ Edition and Child Behavior Checklist were our measure of self-regulation, while cognitive control was measured with the Behavior Rating Inventory of Executive Function (BRIEF). The Screen for Anxiety Related Emotional Disorders (SCARED) was our measure of negative affect. Prior to the mediation model we first established linear relationships between self-regulation and cognitive control or negative affect with Pearson correlations. We then used the average causal mediation effect estimation procedure (with bootstrapping to estimate confidence intervals) to probe whether cognitive control mediated the relationship between negative affect and self-regulation.

Results:

The global executive composite form the BRIEF had medium to large correlations with externalizing behaviors ($r$=.66) and internalizing behaviors ($r$=.46), whereas the total score from the SCARED had similar effect sizes with externalizing behaviors ($r$=.40) and internalizing behaviors ($r$=.78). A subset of children had all 3 measures (n=257), and our mediation model demonstrated that BRIEF scores mediated the relationship between total self-regulation problems on BASC/CBCL and negative affect with a 95% confidence interval of .05 to .13, corresponding to a $p$<0.01.

Conclusions:

Our results demonstrate that both cognitive control and negative affect exhibit significant relationships with self-regulation impairments in a transdiagnostic sample. Furthermore, our mediation results demonstrate that cognitive control explains the relationship between negative affect and self-regulation. Taken together, these results support the RDoC framework as a viable method for examining underlying mechanisms of real world behaviors transdiagnostically.

**172.028 28** Relational Memory Processes in Adults with Autism Spectrum Disorder. M. Ring*, S. B. Gaigg and D. M. Bowler, *City University London*

Background: Previous literature suggests that individuals with Autism Spectrum Disorder (ASD) show mostly intact performance in item memory (Boucher et al., 2005). However, they show particular difficulties with relational memory (Gaigg et al., 2008; Poirier et al., 2011) which is defined as the processing of relations between items and their contexts in order to enable flexible retrieval (Bowler, Gaigg & Lind, 2011) which are functions thought to be supported by the hippocampus (Opitz, 2010). Other theories suggest a problem with the processing of complex information and executive functions, thus implicating the prefrontal cortex (Minshew & Goldstein, 2001). Few studies compare item and relational memory directly and often the item test does not have the same level of complexity/ difficulty as the relational test. Moreover, most previous work has been done using verbal stimulus material or nameable pictures but few have used abstract shapes.

Objectives: In this study we were seeking to compare item memory with different forms of relational memory. Most importantly we were using the same format for all 4 tasks to make the complexity of the item and relational memory tasks more comparable. Stimuli were abstract shapes presented in black and white. All tasks had a working memory component in that items were presented in several shape triplets followed by the test, but only one task involved working memory load in the testing phase as well, in order to investigate the above mentioned theories more specifically.

Methods: Eighteen adults with ASD and 18 IQ, age and gender matched TD individuals were tested with a paradigm adapted from Konkel et al. (2008). In the study phase, which was the same for all 4 tasks, participants were presented with a series of shape triplets. The shapes of a triplet appeared one after the other in specific screen locations (e.g. top right). During test trials, participants received either a repeated or a manipulated set of previously studied triplets. In the *item test* participants were asked to indicate if they had seen an item triplet before when they were presented either with the same 3 items as in the study phase (repeated) or with 1 old and 2 new items (manipulated). In the *relational tasks*no new items were presented keeping either the locations, order or item-combination the same (repeated) or mixing them up (manipulated). Measures taken were percentage of correct answers, hit rate, false alarm rate and hits minus false alarms.

Results: Contrary to our predictions there were significant differences between groups in all measures (except hit rates). Inspection of effect size shows the biggest effect for the location task, followed by the order test, the item test and the item-combination task.

Conclusions: Results suggest item memory impairments when items have to be manipulated. They provide support for both theories and will be discussed in relation to the role working memory processes might play during the encoding and retrieval of item and relational information in ASD.

**172.029 29** Cognitive/ Affective Mechanisms Underlying the Anger Superiority Effect in Children with Autism Spectrum Disorders. T. Isomura*, S. Ogawa and N. Masataka, *Primate Research Institute*

Background: An atypical face and emotion processing in ASD have received wide attention in the research of cognitive characteristics in ASD. It is, however, still not clear whether/ how their processing is different from typical people. In the current study, we focused on the "anger superiority effect (ASE)", which refers a phenomenon where an angry face is detected more quickly than a happy or neutral face in a crowd of distracter (i.e., Face-in-crowd task). This is believed to stem from the attention-getting properties in such threatening stimuli. Previous studies reported that individuals with ASD also showed the ASE but the effect was weaker at a larger crowd size in ASD. (Ashwin *et al.*, 2006; Krysko & Rutherford, 2009). Moreover, children with ASD showed a developmental

change in ASE, but such developmental change was not observed in typically developing (TD) children (Isomura *et al*., submitted). These findings suggested that the rapid processing to angry faces in ASD would be acquired through their development. One remaining question is whether the rapid processing to angry faces in ASD is brought by the same mechanisms as the one typical people use, or it stems from a different strategy.

Objectives: In this study, we examined the cognitive/ affective mechanisms underlying the ASE in children with and without ASD. We focused on configural/ local bias in their face processing.

Methods: 22 children with ASD and 25 TD aged 8 to 12 years old participated in this study. To examine whether they rely more on configural or on local biased processing during a face-in-crowd task, we employed a recognition task in combination with a face-in-crowd task. We used schematic facial stimuli including angry, happy, and neutral faces. Their responses were recorded through a touch sensitive monitor. In the baseline trials, participants were required to touch a discrepant face (angry or happy) among neutral faces as quickly as possible (face-in-crowd task). In the test trials, the face-in-crowd task was immediately followed by a recognition task where the participants were additionally required to recognize the target face that they had detected in the preceded face-in-crowd task. In the recognition task, either whole faces or only local-features of faces (i.e., eyebrows or mouth) were presented randomly.

Results: The quicker detection of angry faces over happy faces was observed along with previous studies. More interestingly, while TD children showed slower reaction time in recognizing local-features compared to whole faces, ASD children did not show such a difference. This suggests that recognizing local-features was as easy as recognizing whole faces in ASD.

Conclusions: These results suggested that children with ASD focused more on local-features during face-in-crowd task than TD children, who relied on configural feature in face processing. Therefore, the mechanisms behind the emotion processing seem different between groups even though they show ASE similarly. Together with previous studies, our results suggest that ASD children, who rely on local-features in processing faces, compensate the poorer face perception, develop emotion process, and successfully detect angry faces quickly as they grow up.

**172.030 30** Deficits in Auditory Temporal Processing Are Associated with Language Impairments in Children with ASD. J. H. Foss-Feig*[1], R. L. Johnston[2], K. Schauder[3], N. de la Fontaine[4], A. P. F. Key[1], M. T. Wallace[1] and W. L. Stone[5], (1)*Vanderbilt University*, (2)*Vanderbilt University Medical Center*, (3)*University of Rochester*, (4)*Yale University*, (5)*University of Washington*

Background: Sensory processing abnormalities are amongst the most commonly reported symptoms associated with autism spectrum disorders (ASD), and are now included in diagnostic criteria for ASD in the DSM-V. Auditory processing is a particular area in which both clinical report and experimental evidence indicate atypicalities in ASD, yet much research is needed to characterize the nature and extent of abnormalities. It has recently been proposed that a diffuse deficit in temporal processing could underlie core symptoms of ASD. Along these lines, our group has shown impairments in the ability of children with ASD to resolve the temporal order of two auditory stimuli presented sequentially at brief intervals. Auditory processing, and auditory *temporal* processing in particular, have been linked to speech perception and language functioning, two areas that are impacted in ASD. Thus, in the present study, we assess auditory temporal processing and examine the extent to which it is related to language functioning in children with ASD.

Objectives: The aims of this study are to determine whether: 1) children with ASD demonstrate deficits, relative to children with typical development (TD) on a task assessing auditory temporal processing; and 2) auditory temporal resolution is related to measures of language functioning among children with ASD.

Methods: Participants included 24 children with ASD and 27 children with TD, all between 10 and 13 years of age. Children completed a psychophysical thresholding procedure to determine the minimum temporal gap within a stimulus that was needed for them to perceive the interruption (i.e., that the stimulus was not continuous). A staircase procedure manipulated

gap size with decreasing step sizes and sequential reversals to converge upon a gap detection threshold for each child. To assess language functioning, children were administered subtests from the Clinical Evaluation of Language Fundamentals–Fourth Edition (CELF-4) and the Comprehensive Test of Phonological Processing (CTOPP).

Results: Results revealed that children with ASD had significantly higher auditory gap detection thresholds than TD children ($p$=0.027). Specifically, whereas TD children needed silent intervals of 3.25ms to reliably detect the presence of gaps in auditory stimuli, children with ASD needed gaps of 3.92ms, on average. The difference between groups reflects a 20.6% increase in gap detection threshold in children with ASD, relative to those with TD. Regarding relations to language functioning among children with ASD, a statistically significant correlation was found between auditory gap detection threshold and scores on the CTOPP Blending Words subtest ($r$= -0.44, $p$=0.03). Thresholds were also correlated significantly with raw scores from the Concepts and Following Directions ($r$= -0.41, $p$<0.05), Word Classes–Receptive ($r$= -0.67, $p$<0.001), and Word Classes–Expressive ($r$= -0.49, $p$=0.02), subtests of the CELF-4.

Conclusions: Results of this study revealed increased auditory gap detection thresholds in ASD relative to TD controls, suggesting impairments in auditory temporal processing. Among children with ASD, greater difficulty with auditory gap detection was associated with more substantial language-related impairments. These findings provide clues into the etiology of language-based deficits in ASD, and suggest avenues for future research and treatment approaches.

**172.031 31** Central Tendency Effects in Temporal Interval Reproduction in Autism. T. Karaminis*[1], L. E. Neil[1], G. Cappagli[1], D. Aagten-Murphy[2], G. M. Cicchini[3], D. Burr[2] and E. Pellicano[1], (1)*Centre for Research in Autism & Education, Institute of Education*, (2)*University of Florence*, (3)*Consiglio Nazionale delle Ricerche*

Background:

Central tendency, the tendency of judgements of quantities (of length, duration, number, color etc.) to gravitate towards their mean value, is one of the most robust effects in perception. In the temporal domain, duration estimates of the same time intervals are shorter or longer depending on whether they are presented in the context of short or long intervals. A computational Bayesian approach has recently been shown to predict this effect in temporal reproduction. According to this model, the central tendency effect reflects the extent to which internal representations of a mean value (prior knowledge about temporal statistics) are integrated with sensory estimates (the likelihood of observations) to generate a final (posterior) perceptual judgement. The more noisy and ambiguous the sensory estimates, the more final perceptual judgements rely on prior knowledge. Priors therefore improve the efficiency of computations by reducing overall noise or error.

A recent theoretical account proposed that attenuated Bayesian priors might be responsible for the unique perceptual experience of autistic people, leading to a tendency to perceive the world more accurately rather than modulated by prior experience. We therefore predicted that children with autism should present reduced central tendency effects compared to typically developing (TD) children of similar age and ability.

Objectives:

We sought to test this Bayesian model of autistic perception by comparing central tendency effects in children with autism and TD children and modelling their patterns of performance based on an existing computational model.

Methods:

In an ongoing study, 13 children with autism, aged between 7 and 14 years, and 44 TD children of similar age and ability received two child-friendly tasks, modified from existing studies: (1) a "Ready, Set, Go!" temporal reproduction paradigm with two interval ranges (1006-1536 msec and 1270-1800 msec) and (2) a temporal discrimination task (comparison stimulus of 500 msec). Sixteen typical adults also took part. We compared the three groups on their central tendency effects and on the reliability and accuracy of their temporal estimates. We performed simulations with the Bayesian model to estimate the form of participants' prior knowledge and how this compares to that required for optimal computations.

Results:

Analyses showed a general trend of increased central tendency in children with autism compared to TD children and adults, as well as less reliable and less accurate temporal judgements. Similar differences were seen between TD children and adults. Model simulations suggested that children with autism and TD children generated perceptual judgements based on representations of prior knowledge that were more broad than adults, and in a non-optimal manner.

Conclusions:

We show here that the tools of Bayesian inference can be used to model typical children, adults, and autistic children's temporal reproduction performance. We further demonstrate the, contrary to predictions, children with autism and TD children weight prior knowledge and sensory estimates in a similar fashion.

**172.032 32** Encoding Similarities but Recognition Differences in Eye-Movement Behaviour during Face Emotion and Identity Processing in Autism Spectrum Disorder. H. E. Matheson*, J. H. Filliter, P. A. McMullen and S. A. Johnson, *Dalhousie University*

Background: Individuals with Autism Spectrum Disorder (ASD) show a number of face processing deficits compared to typically developing controls (TYP). These deficits may result from impaired processing of a number of cognitive domains including basic perceptual processes.

Objectives: We sought to investigate, using objective measures of eye-movement behaviour, the visual processing strategies of individuals with ASD during different tasks of face processing to determine whether basic perceptual processes are disrupted.

Methods: We used eye-tracking technology to measure eye movement behaviour or a group of individuals with ASD ($N$ = 8) and TYP ($N$ = 24) in a) an emotion judgment task, b) an identity judgment task, and c) a picture judgment control task. Participants saw sequential pairs of faces (with a 1000 ms delay) and made same/different judgments on the pairs. We presented the basic emotional expressions in all tasks.

Results: Our main finings show that a) individuals with ASD rely less on the upper region and more on the lower region of faces, b) both groups show a smaller reliance on the upper region when making emotion judgments than when making identity judgments, c) that face emotion modulates the relative reliance on the upper region for both groups, and d) that ASD and TYP show similar patterns of eye movement behaviour at encoding, but differences at recognition.

Conclusions: These results further specify the nature of face processing deficits in ASD, and suggest that perceptual processes are preserved at encoding but disrupted at recognition in individuals with ASD.

**172.033 33** Evidence for Dissociable Visual Perception and Executive Functioning Processes in Typically Developing Adults with Varying Degrees of Autistic-like Characteristics. R. J. Clements[1], K. B. Parkington*[1], O. Landry[2] and P. Chouinard[3], (1)*Dalhousie University*, (2)*McMaster University*, (3)*The Unversity of Western Ontario*

**Background:** The ability to recognize differences between visual stimuli has been noted as a particular strength for individuals with an Autism Spectrum Disorder (ASD), as well as for adults with varying degrees of subclinical autistic-like characteristics. Alternatively, executive functioning processes have been demonstrated to be a relative weakness for these individuals. Limited research is currently available investigating the interaction between visual perception and executive functioning, particularly in an ASD or subclinical population.

**Objectives:** The aim of the current study was to investigate the relationship between visual perception and executive functioning processes in a subclinical group of adults along the Autism-Spectrum Quotient (AQ) range.

**Methods:** One hundred typically developing adults with scores across the AQ range completed an implicit association learning task that involved mapping four distinct visual stimuli on to four unique button responses. Half of the participants completed the implicit association learning task with novel symbols (i.e., control condition), whilst the remaining participants were familiarized with the test stimuli prior to the learning task to eliminate any potential perceptual strategies (i.e., familiarization condition). Participants completed the implicit association learning task to a point of overlearning, and the number of trial bins

required to reach a 90% accuracy criterion was established using logarithmic transformations.

**Results:** Univariate regression analyses revealed that learning performance in the control condition increased in accordance with AQ score, such that individuals with higher AQ scores were more likely to learn the implicit association task faster than participants with lower AQ scores when awarded an inter-stimulus perceptual advantage. However, when participants were no longer awarded a perceptual advantage in the familiarization condition, implicit association learning showed the opposite pattern, such that performance was hindered for participants with high AQ scores and enhanced for participants with low AQ scores. The Attention to Detail subscale of the AQ was found to be significantly related to performance in the control condition, supporting the perceptual advantage hypothesis. Performance for participants in the familiarization condition was significantly related to the Social Skills subscale, and a trend was found for the Attention Switching subscale, suggesting that additional factors may play a role in implicit association learning.

**Conclusions:** These findings confirm the visual perception advantage and executive functioning deficit in individuals along the AQ spectrum, and are the first to demonstrate a double dissociation model for visual perception and executive functioning in this population. These findings are discussed in relation to potential models for visual perception and executive functioning in typical and ASD populations.

**172.034 34** Eye-Tracking Measures of Executive Functioning Correlate with Academic Achievement in Adolescents with ASD. L. Hall*[1], E. A. Kelley[1], D. E. Wilson[1], E. Ladwig[1], R. Furlano[1] and J. Rajsic[2], (1)*Queen's University*, (2)*University of Toronto*

Background: Executive functioning (EF) is a set of higher order cognitive processes that involve inhibition, cognitive shifting, and working memory. A connection between executive functioning and academic achievement has been identified in typically developing (TD) adolescents. The relationship of EF with academic achievement is relevant to clinical populations that have difficulties in these areas, such as individuals diagnosed with autism spectrum disorder (ASD).

Objectives: The current study aims to extend our understanding of cognitive and academic difficulties among adolescents with ASD by investigating the correlations between an eye-tracking measure of executive functioning ability and academic achievement. Findings will help clarify the nature of the relationship between cognitive and functional deficits in adolescents with ASD.

Methods: Data collection was conducted on 40 adolescents (20 ASD and 20 TD), 11-18 years of age. The ASD and TD groups were matched on cognitive age. The Eyelink 1000 eye tracking system was used to collect data on saccadic eye-movements during a memory-guided eye-tracking task. This task is reflective of working memory and shifting abilities. Academic achievement was assessed using the Woodcock-Johnson III Tests of Academic Achievement. Specifically five subtests were selected from this battery: Story Recall, Understanding Directions, Writing Fluency, Math Calculations, and Math Fluency.

Results: Partial correlations were conducted to assess whether the percent of saccadic eye-movement errors during the memory-guided task was correlated with the five subtests of academic achievement for both the ASD and TD groups while controlling for the effect of full-scale IQ. For the ASD group, percent of saccadic errors significantly negatively correlated with Math Calculations scores ($r$ = -.54, $p$ = .03) and Math Fluency scores ($r$ = -.69, $p$ = .002), and also negatively correlated with Writing Fluency scores ($r$ = -.47, $p$ = .06) with marginal significance. For the TD group, percent of saccadic errors was only significantly negatively correlated with Math Calculations scores ($r$ = -.51, $p$ = .04).

Conclusions: Working memory and shifting ability, as assessed using eye-tracking technology, is significantly related to academic achievement across a number of domains in adolescents with ASD. Specifically, for adolescents with ASD, an increase in errors on the delayed-memory eye-tracking task corresponded with a decrease in math- and fluency-based academic achievement. These findings, along with further investigation regarding this relationship, may help to clarify the nature of the development of academic abilities in ASD.

**172.035 35** Grouping Interference in ASD: Evidence from a Series of Multiple Object Tracking Experiments. R. Van der Hallen*[1], K.

Evers[1], L. de-Wit[1], B. Haesen[1], J. Steyaert[2], I. Noens[1] and J. Wagemans[1], (1)*KU Leuven*, (2)*University of Leuven*

**Background:** In autism spectrum research both atypical perceptual organization and inadequate motion perception have been a major topic of interest. While some studies find superior processing of local details, substandard processing of global structures, reduced sensitivity to biological motion or heightened thresholds for coherent motion in individuals with ASD, research findings on these phenomena vary widely and are often contradictory.

**Objectives:** In order to gain insight into these controversial phenomena, we performed a series of experiments using a modified version of the Multiple Object Tracking paradigm as designed by Scholl et al. (2001). Previously administered to adults only, MOT was designed to evaluate, in an implicit manner, to what extent grouping cues hamper tracking performance. With these experiments, we aimed to investigate the effect of connection-based grouping in typically developing (TD) children, and whether connection-based grouping had a differential effect in children with ASD.

**Methods:** In two behavioral experiments we presented a modification of the MOT paradigm to a group of children with ASD and to an age- and ability-matched TD group (Study 1: 6 to 10 years old, Study 2: 8 to 12 years old). In both cases participants were asked to track and distinguish four randomly moving targets from four distracters. While Study 1 administered one ungrouped and one grouped condition, Study 2 administered one ungrouped condition and two grouped conditions (visually connected with randomly placed lines vs. visually connected as closed contour). Note the ratio of ungrouped vs. grouped trials is different for Study 1 (ratio 1:1) than for Study 2 (ratio 1:2).

**Results:** Overall, no group difference was found comparing children with and without ASD: both participant groups showed adequate tracking abilities and both performed less in the grouped condition(s) than in ungrouped condition. However, while Study 1 found a reduced hampering effect of grouping in children with ASD compared to TD children, Study 2 failed to replicate this finding. In addition, Study 2 did not reveal any within or between group differences for both grouping conditions (randomly connected vs. connected as a closed contour). With regards to overall MOT performance, correlations were found with general Social Responsiveness Scale scores for both the TD and ASD group.

**Conclusions:** Firstly, the present experiments demonstrate that grouping cues have a similar impact on tracking performance in TD young children, as what was previously shown in TD adults. Secondly, results reveal mixed evidence in terms of the hampering effect of grouping cues on tracking ability in ASD. A significantly reduced interference effect of grouping in ASD was only found in the case of an equal distribution of ungrouped vs. grouped trials. Results suggest that atypical visual processing in ASD is dependent on the specific task and stimulus set. Our results challenge the idea of a general visual processing *deficit* in ASD, but point in the direction of a qualitative difference in visual processing.

**172.036 36** Drawing Corners: Using a Drawing Reproduction Task to Test Theories of Local-Global Processing in Children with Autism. L. Kenny*[1], A. D. Smith[2], A. Rudnicka[1] and E. Pellicano[1], (1)*Centre for Research in Autism & Education, Institute of Education*, (2)*University of Nottingham*

**Background**: Much research attention has centred on strengths and weaknesses in local-global processing in individuals with autism. On some accounts, individuals with autism excel at local processing at the cost of global processing. On other accounts, autistic perception is characterised by enhanced local processing without any impairment in integrative processing. Although drawing is usually examined in relation to autistic savant abilities, it can also greatly inform our understanding of autistic perception. Studies of drawing reproduction in autism, however, have yielded mixed results and, to our knowledge, have not investigated local and global processing in relation to perceptuomotor coding of spatial relations.

**Objectives**: The current study investigated local and global processing in children with and without autism by examining their perceptuomotor representations of object relations in a drawing task. Specifically, we examined children's between-object coding skills (local processing) and their within-object coding skills (global processing) by assessing drawing accuracy as they copied simple hierarchical geometric figures. Perceptual grouping cues were manipulated by altering elements of the figures such that some

figures were more likely to group into a coherent global form than others.

**Methods**: Participants were 24 children with autism and 24 typically developing children matched on age, gender and ability. They completed a copying task comprising 24 trials presented in a randomised order. On each trial, participants copied a set of four corners arranged to form a 6cm x 6cm square. In order to examine the relationship between perceptual grouping cues and drawing accuracy we manipulated the size (0.5cm, 1.5cm or 2.5cm), orientation (rotated clockwise or anticlockwise by 10°), and number of rotations (2 or 4) of the corners in each trial. We coded each participant's drawings following procedures outlined in a previous experiment with constructional apraxia patients.

**Results:** There were two indices of global processing: (1) a measure of global shape accuracy (based on the internal angles of the copy produced by participants) and (2) the extent of deviation from a 1:1 height/width ratio (i.e., to form a square as opposed to a rectangle). Children with autism made more errors in their reproductions of the global shape than typical children. For children with autism, we also found that changes in orientation of the corners disproportionately affected the global reproduction of figures. There were no significant group differences in the reproduction of the individual (local) elements.

**Conclusions:** The current results suggest that children with autism show difficulties reproducing the spatial relations between the elements when the individual corners do not form a strong perceptual whole – consistent with accounts that postulate global processing difficulties in autism. This may suggest that children with autism rely more on grouping cues than what has been previously reported in the literature.

**172.037 37** I Know It's Heavy but I Can't Make Anything of It before I Feel It. M. Martel*[1], S. Sonié[2], E. Pirat[3], B. Kassai-Koupai[3], C. Schmitz[2] and A. C. Roy[1], (1)*L2C2 - UMR 5304 - Institute of Cognitive Science*, (2)*Lyon Neuroscience Research Center*, (3)*Center for Clinical Investigation of Lyon - EPICIME*

**Background:** A trustworthy representation of oneself and the world around us necessarily relies on a functional sensorimotor system. ASD children who suffer from a wide range of symptoms, from social communication impairments to restricted, repetitive patterns of behavior (DSM V), often exhibit an atypical sensorimotor development.

**Objectives:** To determine the nature and the specificity of motor deficits in ASD, we compared both feedforward and feedback mode of controls in healthy children and ASD children. We investigated the motor development of healthy children aged from 5 to 10 years-old and ASD children aged 9-10 years-old.

**Methods:** Children were required to reach and grasp an object in order to displace it to a lateral location. The objects, two visually identical opaque bottles, could be heavy or much lighter. We manipulated the participant's previous knowledge of the object weight: when known, participant might anticipate the consequences of the weight when reaching for the object, prior to contact with it, thus allowing for feedforward control. Conversely, when unknown prior to contact, participants had to adapt to the object weight after contact (feedback control), in the displacing phase of the movement. Movement kinematic was recorded with a high-resolution optoelectronic motion tracking system.

**Results:** Neurotypical children were able to use weight information beforehand as early as age 5: they showed peaks of longer latencies and smaller amplitudes for heavy objects during the reaching phase. Children from 7 to 10 years-old also used weight information beforehand, but exhibited an opposite and more efficient pattern to overcome its effects (shorter latencies and higher peaks for heavy objects). When unknown, the heavy object impacted the displacing phase in the three groups alike: movements were slowed down, displaying later and smaller peaks in the heavy object condition. Preliminary results obtained on 10-year-old children with ASD showed that they were unable to benefit from weight knowledge before they came into contact with the object. Surprisingly though, previous knowledge of object weight was used in the displacing phase enabling the on-line control. In the unknown weight condition in which ASD children had to rely on their on-line control, their performance was comparable to that of healthy children.

**Conclusions:** Our results show that healthy children used a feedforward mode of control since the age of 5, yet this control becomes efficient and adequate only at the age of 7. ASD children

were unable to modulate their movements as a function of the upcoming object weight, showing thus an impaired feedforward control. Interestingly, the displacing phase of the movement after somatosensory feedback differed between known and unknown weight conditions, thus testifying that ASD children were nevertheless capable to take weight information into account. These findings shed a new light on the motor control of ASD children by revealing a preserved on-line control and a deviant feedforward mode of control. This incapacity of anticipating their own actions could participate to their trouble in understanding others' actions and behaviors, and therefore could play a role in their lack of communication skills.

**172.038 38** Individual Differences in Implicit Learning Abilities: Implications for Identifying Treatment Predictors. R. Jones*, C. T. Moody, J. Baker, S. Levitt, L. Donnelly and C. Lord, *Weill Cornell Medical College*

Background: Implicit associative learning is an individual's ability to form connections between objects or stimuli without conscious awareness. These skills are critical for navigating the environment as well as higher order cognitive abilities and social communication and language skills.

Objectives: There is inconsistency in the literature as to whether individuals with ASD have difficulties with such learning. Some suggest that there is impairment, while others report no differences compared to typically developing individuals. It is likely that the discrepancy is not simply explained by methodological differences across studies, but reflects variability within ASD for implicit learning. We hypothesize that the children who do not respond to classic behavioral intervention have difficulties with implicit learning.

Methods: Building upon the extensive implicit learning literature, we designed a child-friendly task that measures differences in reaction time (RT) behavior and accuracy to a target stimulus predicted by two cues at differing probabilities. In each trial, children were instructed to touch a target image presented on an iPad but to refrain from touching the cues and distractor image. Unbeknownst to the participants, one of the cues predicted the target image at a high probability (75%), while the other cue preceded the target at a low probability (25%); the distractor appeared when the target was not presented. Trials were divided into thirds (early, middle and late) in order to assess learning differences.

Results: Preliminary results (N = 9; 2F; 3-6 years of age) are reported in typically developing (TD) children, typically developing children who have a sibling with ASD, and children with ASD. TD children demonstrated an increase in false alarms (incorrectly pressing the distractor) when presented with the high probability cue versus the low probability cue. TD children who have a sibling with ASD, and children with ASD, make an equal number of false alarms after the two cues. Regardless of diagnosis or sibling affiliation, all children show speeding in reaction times by the late trials to the target when preceded by the 75% cue compared to the 25% cue. Some children, regardless of age, demonstrate this pattern during early trials, suggesting individual differences in implicit learning.

Conclusions: Preliminary data suggest the ability to form associations during an implicit probabilistic learning task is variable in young children and may differ in the broader autism phenotype. Individual differences in how quickly children learn the patterns may be important for predicting intervention success in young children with ASD. Future testing in the three groups will further categorize individual variability in implicit learning abilities both within and across groups of children.

**172.039 39** No Evidence for Deficits in the Multisensory Integration of Self-Generated Movement in Children with Autism Spectrum Disorder. M. Jaime*[1], J. Longard[2], S. E. Bryson[3] and C. Moore[2], (1)*Indiana University-Purdue University Columbus*, (2)*Dalhousie University*, (3)*Dalhousie/IWK Health Centre*

Background: Previous studies have reported atypical neurophysiological and perceptual processing of auditory, tactile, and visual stimulation in individuals with autism spectrum disorder (ASD). Auditory-visual and auditory-somatosensory temporal binding deficits have also been demonstrated in ASD. However, no research has explored the ability of children with ASD to integrate temporally asynchronous visual-proprioceptive feedback.

Objectives: To examine the multisensory integration of self-generated movement in children with ASD.

Methods: Seventeen children with ASD between 7 and 11 years of age and 20 typically developing children matched for age, verbal IQ and performance IQ manipulated a joystick with their right hand. Children in both groups were only able to see their joystick movements via a computer monitor which displayed real time video captures of their movements in a live or delayed format. During familiarization, the live and delayed (3 seconds) video captures were explained to the children as *happening now* or *happening later*. In the subsequent pre-test phase, the video captures were randomly switched between the live and 3 second delayed presentation and children were asked whether the video captures were happening *now* (live) or *later* (delayed). The order of presentation was semi-randomized, so that each participant received one of two possible orders. To establish that each child understood the difference between live and delayed video captures, a criterion of 5 consecutive correct answers had to be met in order for the experiment to continue to the test phase. In the test phase, children were again asked to judge whether the video captures were happening *now* (live) or *later* (delayed); however, delay durations were reduced to 0 ms, 100 ms, 200 ms, and 300 ms. Trials were also semi-randomized, so that each participant received one of two possible orders.

Results: Across diagnostic groups, children made more delay judgments as a function of increasing delay duration, $F(3, 33) = 63.4$, $p < .001$, $\eta_p^2 = 0.644$. However, performance on the task did not differ significantly between diagnostic groups, $F(3, 33) = .213$, $p = .887$, $\eta_p^2 = 0.006$, suggesting that children with ASD integrated visual-proprioceptive feedback as effectively as the typically developing children.

Conclusions: Our current findings provide evidence that children with ASD effectively integrate asynchronous visual and proprioceptive feedback. This raises the questions of whether previously reported multisensory temporal binding deficits in ASD generalize to visual-proprioception and whether visual-proprioceptive integration may be enhanced at the expense of multisensory integration of other modalities in ASD.

**172.040 40** Predictors of Basic Reading Skills in High-Functioning Children with Autism Spectrum Disorder. P. Kittel* and C. A. Stone, *University of Michigan*

Background: The number of high-functioning children identified with Autism Spectrum Disorder (ASD) has greatly increased in recent years. The academic skills of these children show considerable variation; although word reading skills are often comparable, and sometimes superior, to those of typically developing children, some children struggle (Nation, Clarke, Wright & Williams, 2006). It is important to update and expand our understanding of factors contributing to the development of basic reading skills because revised diagnostic criteria, small samples, large age and ability ranges, and varying outcome measures may limit the generalizability of older results.

Objectives: The purpose of this study was to document basic reading, cognitive and language skills in high-functioning children with ASD in the early grades and identify predictors of basic reading skills, such as executive functions and cognitive and language abilities. Measures of cognitive flexibility were included as possible factors in the acquisition of reading since relationships between cognitive flexibility and reading have been reported for typically developing children (Cartwright, 2008), and children with ASD exhibit deficits in cognitive flexibility (Ozonoff, 1997).

Methods: Cognitive flexibility, literacy, language, and cognitive abilities were assessed in 63 children with ASD ages 6 through 9 using the Woodcock Johnson III and the Wisconsin Card Sorting Test. All participants had nonverbal ability above 80, were enrolled in grades 1 - 4, and participated in the general curriculum. The sample was diverse for race, sex, parent education, community size, and educational program. A series of regression analyses was conducted to determine predictors of basic reading and whether cognitive flexibility explained any additional variation.

Results: Basic reading skills varied greatly, with many children, especially first-graders, exhibiting above-average skills. Verbal, nonverbal, language, phonemic awareness, and word reading skills were average for the group, but weaknesses were found in cognitive flexibility, cognitive efficiency, working memory, visual processing speed, listening comprehension, and retrieval fluency.

Predictors of basic reading skills frequently noted in the literature, such as nonverbal ability and phonemic awareness, had strong relationships with the basic reading measures. Moderate relationships were found with verbal ability, oral language, and working memory.

Cognitive, language, and phonemic awareness skills predicted basic reading to a similar extent as in typically developing children. Specifically, five nonverbal, language, and phonemic awareness tests were able to predict 55 percent of the variance in word reading skills. Measures of cognitive flexibility did not contribute significantly to a regression model that included these other factors.

Conclusions: Most high-functioning children with ASD in the early grades have good word reading skills, and predictors of reading are similar to those found in typically developing children. However, children with average verbal and nonverbal skills generally exhibit weaknesses in cognitive efficiency, cognitive flexibility, working memory, and listening comprehension. Specialized instruction and accommodations for children with ASD, even those with above-average ability, are needed to address the impact of these weaknesses on academic learning and school success. Further research is needed to determine whether word reading performance declines over time compared to age peers.

**172.041 41** Reading Comprehension Impairments in Higher Functioning School-Aged Children with ASD. N. S. McIntyre*[1], S. Novotny[1], L. E. Swain-Lerro[1], J. S. Beck[1], M. Montanez[1], T. M. Oswald[1], M. Solomon[2] and P. C. Mundy[1], (1)*UC Davis*, (2)*MIND Institute*

Background:

The development of adequate reading comprehension by the end of the elementary school years is essential to subsequent academic achievement, cognitive development, and ultimately vocational success (National Reading Panel, 2000). Recent research has raised the hypothesis that reading comprehension impairment may be part of the social communication phenotype of higher functioning school-aged children with ASD (Norbury & Nation, 2011; Randi, Newman, & Grigorenko, 2010; Ricketts et al., 2013).

Objectives:

This study was designed to assess reading comprehension, its component skills, and possible moderating factors such as comorbid ADHD, in a large sample (N=79) of younger (8-11 yo) and older (12-16 yo) higher functioning students with ASD (HFASD; FSIQ>75) using measures of text level comprehension and word level processing.

Methods:

The HFASD sample was compared to an age-matched Control sample (N=83), half of which had elevated ADHD symptoms. Reading comprehension was measured with the standardized GORT-5 and a curriculum-based assessment, the QRI-5. Component/word level skills were assessed with the following scales: TAPS-3 Auditory Reasoning (AR); CTOPP for Elision, Nonword Repetition, Rapid Digit/Letter Naming; TOWRE-2 Sight Word Efficiency (SWE), Pseudoword Efficiency (PDE); Derivational Morphology (J. Carlisle, 2000); CELF-4 Recalling Sentences (RS); WIAT Receptive Vocabulary. The WASI was administered for IQ and Expressive Vocabulary; the ADOS-2 for ASD confirmation; the Conners-3 for ADHD symptoms.

Results:

All analyses included FSIQ as a covariate. The results revealed that the HFASD sample scored significantly lower than Controls on GORT Comprehension, $p<.000$, $eta^2 = .091$; QRI Comprehension, $p=.002$, $eta^2=.065$; CELF Recalling Sentences, $p<.000$, $eta^2=.088$; Morphology, $p=.008$, $eta^2=.048$; Receptive Vocabulary, $p=.022$, $eta^2 = .036$; and Expressive Vocabulary, $p=.002$, $eta^2=.063$. There was no significant effect of Diagnostic Group on the remaining word level processing measures.

Analysis of GORT Comprehension Grade Equivalent scores revealed that, on average, younger children with HFASD (8-11 yo) obtained scores 1.3 grades below grade-level and older children with HFASD (12-16 yo) scored 2.4 grades below. In the total HFASD sample, 27% of the children scored >3 grades below grade-level. The subgroup with ADHD T-scores > 70 had lower QRI Comprehension scores in the Control but not the HFASD sample, $p=.005$, $eta^2= .055$. In the HFASD sample, ADOS-2 Total scores were significantly correlated with GORT Comprehension, $r= -.319$, $p=.008$; QRI

Comprehension, r= -.247, p=.038; TAPS Auditory Reasoning, r= -.228, p=.05.

Conclusions:

Students with HFASD may be vulnerable to reading comprehension impairments and cross-sectional data suggests that the expression of this vulnerability increases with age and development. They may also be vulnerable to language impairments in both semantic and structural/syntactic domains. HFASD children appeared to be less vulnerable to developmental impairment in word level processing. Word level skills were a relative strength and not significantly different than those of their same-age peers. The significant relations between both reading comprehension measures, the auditory reasoning measure, and ADOS scores was consistent with the hypothesis that their reading disturbance may be a part of the social communication phenotype of higher functioning school-aged children with ASD.

**172.042 42** Social Attention, Higher Functioning ASD, and ADHD Symptoms. S. Novotny*[1], W. Jarrold[2], N. S. McIntyre[2], L. E. Swain-Lerro[2], T. M. Oswald[2], M. Solomon[3] and P. C. Mundy[2], (1)*University of California, Davis*, (2)*UC Davis*, (3)*MIND Institute*

Background: Autism Spectrum Disorder is characterized by deficits in social attention. However, it may not be possible to unambiguously identify attention deficits in studies of higher functioning children because many of these children also present with elevated symptoms associated with ADHD.

Objectives: The goal of this study was to compare attention and social attention in higher functioning children with ASD (HFASD), who exhibited either low or high levels of ADHD symptoms.

Methods: Four groups of school-aged children participated in this study: 45 with HFASD, 19 with HFASD and ADHD, 36 with ADHD but not ASD, and 39 with typical development. The groups were matched on age (means = 11.3, 10.9, 11.9, 11.7 respectively) but not on IQ (means = 104, 96, 101, 114). As a result, IQ was used as a covariate in all analyses. The groups also differed on parent report of ASD symptoms, as measured by the SCQ and SRS, as well parent report of ADHD symptoms, as measured by the Conners-3 ADHD Total t-scores (70.2, 84.6, 75.2, 49.5). Attention was assessed while children viewed a virtual classroom with 9 targets around a large table (one central target, 3 targets at intermediate positions left and right of center, and one target at an extreme position left and right of center). The task included three 3 minute conditions: 1) a Non-Social (NS) condition, during which children looked at 9 "lollipop" shaped forms around the table, 2) a Social Condition (SC), during which children looked at 9 avatar "peers", and 3) a High-Demand Social Condition (HDSC), during which the avatars faded away if the child did not fixate them frequently.

Results: Analyses revealed diagnostic groups effects in all conditions for average duration of target fixations: NS, $F(12, 304) = 2.08$, $p < .05$, $eta^2 = .07$, SC, $F(12, 304) = 2.21$, $p < .03$, $eta^2 = .07$, and the HDSC, $F(12, 304) = 2.08$, $p < .015$, $eta^2 = .08$. In the NS and SC, the ADHD group displayed longer fixations to the center target than did the other groups, the TD group displayed longer fixations to the intermediate targets than the other groups, and the HFASD groups displayed shorter fixations to all but the extreme targets relative to the other groups. On the HDSC task, the HFASD-ADHD group displayed a unique pattern of longer duration fixations to the central avatar and much shorter fixations to the intermediate targets than the other groups.

Conclusions: The results of this study indicate that individuals with HFASD, HFASD-ADHD and ADHD may all display patterns of attention that distinguish them from their typically developing peers on this task. In particular, the HFASD groups displayed lower duration, more fleeting attention to social *and* non-social stimuli relative to the other groups. This tendency was exacerbated in the HFASD-ADHD group in the HDSC task, suggesting this sub-group may be especially vulnerable to increased demands in attention tasks.

**172.043 43** The Association of Child Characteristics on Outcome in a School-Based Behavioral Intervention. M. Pellecchia*[1], J. E. Connell[2], M. Xie[1] and D. S. Mandell[1], (1)*University of Pennsylvania School of Medicine*, (2)*Drexel University*

Background: Although interventions based on the principles of applied behavior analysis have been repeatedly cited as evidence-based for individuals with autism, significant discrepancies in outcome are evident within the literature. That is, in most

studies evaluating intervention outcomes for students with ASD, some students make significant progress, while others make minimal to no progress. The baseline differences in children's clinical characteristics have been hypothesized as an important predictor of treatment outcome. Few studies, however, have had the sample size, a controlled treatment environment, and the careful characterization of children needed to address this question.

Objectives: The primary goal of this study was to identify individual characteristics that predicted differences in outcome for elementary-school-age children with autism. Specifically, the study evaluated differences in outcome following one year of a behaviorally-based intervention as a function of children's cognition, challenging behavior, language ability, autism severity, social skills, adaptive behavior, co-morbidity of psychological diagnoses, and restrictive and repetitive behavior.

Methods: The sample included 368 students with autism in kindergarten-through-second-grade classrooms in a large urban school district that participated in an intervention study. As part of the intervention study, students received instruction using the Strategies for Teaching Based on Autism Research (STAR) program as part of their classroom routines. The STAR program is a behaviorally based program that comprises Discrete Trial Training, Pivotal Response Training, and Teaching within Functional Routines. Intervention fidelity was measured monthly via fidelity checklists and observations by trained recorders. Data were collected at the beginning and end of the school year. Measures were completed by teachers, parents and direct observation, and included the Differential Ability Scales, 2nd edition; Aberrant Behavior Checklist; Adaptive Behavior Assessment System, 2nd edition; Autism Diagnostic Observation Schedule; Child Symptom Inventory; PDD Behavior Inventory; and Social Responsiveness Scale. The outcome of interest was change on the Differential Abilities Scale. Linear regression with random effects for classroom and student were used to evaluate the association between change in outcome and baseline variables of interest following one year of intervention.

Results: Analyses are ongoing. Preliminary adjusted analyses indicate that higher expressive language skills at the start of the year were associated with improved outcome. Increased anxiety was associated with poorer outcomes. No other child-level variables were associated with outcomes.

Conclusions: The finding that children with greater expressive language skills at the start of the intervention year had better outcomes, on average, than other children is in keeping with prior research. These results may imply that an earlier focus on improving language skills in young children with autism could lead to improved outcomes for these students. The finding that children with greater anxiety were more likely to have poorer outcomes is novel, and suggests the importance of identifying and treating anxiety symptoms early. The finding that other variables such as baseline cognition, autism severity, challenging behavior, adaptive behavior, and social skills were not associated with outcome is promising, and suggests the broad benefit of behavioral approaches to early elementary education of children with autism.

**172.044 44** Writing Development and Working Memory in School-Age Children with ASD. M. C. Zajic*, N. S. McIntyre, L. E. Swain-Lerro, S. Novotny, T. Kapelkina, T. Oswald and P. C. Mundy, *UC Davis*

Background: Higher function children with ASD (HFASD) appear to display significant difficulty with written communication (Mayes & Calhoun, 2007; 2008). The factors involved in these writing impairments may involve attention problems (Mayes & Calhoun, 2003) or problems with working memory (Swanson & Berninger, 1996).

Objectives: This study examined the development of writing in children with HFASD in comparison to a sample of children with ADHD, and a typical control sample. The study also examined the potential mediating effects of age, IQ and verbal working memory (VWM) on Diagnostic Group differences in writing performance.

Methods: 27 children with ASD (Age = 10.5 years, IQ = 103, VWM = 4.4) were compared to 21 children with ADHD (Age = 11.9 years, IQ = 103. VWM = 5.6) and 19 children with typical development (Age = 12.5 years, IQ = 116, VWM = 6.6). The Diagnostic Groups differed on IQ ($p < .02$), age ($p < .03$), and VWM ($p < .0005$). These variables were included as covariates in the analyses. ASD was assessed with the Social

Communication Questionnaire and the Social Responsiveness Scale. ADHD was assessed with parent report on the Conners-3. Word Count and Narrative Structure of writing were measured with the Wechsler Individual Achievement Test-III. Verbal working memory was measured with the Wide Range Assessment of Memory and Learning. IQ was measured using the Wechsler Abbreviated Scale of Intelligence-II.

Results: Significant MANCOVA effects of Diagnosis Group were found on the writing variables using IQ or Age as covariates. For example, with IQ as the covariate, there was a significant effect of Diagnostic Group on Word Count, $p < .001$, $eta^2 = .21$, and the effect on Narrative Structure approached significance, $p < .11$, $eta^2 = .07$. Pairwise comparisons indicated that HFASD group was significantly lower than the ADHD group ($p < .05$) and the TD group ($p < .001$) on Word Count. The ADHD group was also lower than the TD group ($p < .05$). Only the ASD group displayed lower Narrative Structure scores than the TD ($p < .03$). Within the Narrative Structure analyses indicated that the ASD group used fewer elaborations than the ADHD group (.43 vs .76), who displayed fewer elaborations than the TD group (.76 vs. .95, $p < .035$, independent samples median test). When the verbal working memory was the covariate, however, none of the diagnostic group differences on writing were significant.

Conclusions: The ASD sample differed in writing from the TD sample on both word count and narrative structure, and from the ADHD sample on word count. These observations suggested that the ASD sample had difficult in generating both written language and coherent structure in written language. The results also suggested that the ASD impairments may have been secondary to problems with verbal working memory. If so, the data raise the hypothesis verbal working memory disturbance contributes to the impaired ability of children with HFASD to generate language and narrative structure in a writing task.

## 173 Genetics

**173.045 45** Association Between GABA(A) Receptor Subunit Polymorphisms and Autism Spectrum Disorder (ASD) in an Argentinean Sample. C. V. Sesarini*[1], L. Costa[1], N. Granana[2], M. Naymark[3], A. R. Cajal[1], M. Garcia Coto[4], R. Pallia[3] and P. F. Argibay[1], (1)*Instituto de Ciencias Basicas y Medicina Experimental (ICBME), Hospital Italiano de Buenos Aires*, (2)*Hospital Durand*, (3)*Hospital Italiano de Buenos Aires*, (4)*CIDEP*

**Background:** Autism Spectrum Disorders (ASDs) can be conceptualized as a genetic dysfunction disrupting brain circuits mediating social cognition and language. Some forms of ASD might be associated with a connectopathy resulting in increases/decreases in neuronal excitability. GABA has been implicated since during development is an excitatory neurotransmitter and in the adult brain GABA acts on the GABA(A) receptor (GABAR) complex and mediates synaptic inhibition.

**Objectives:** To study single-nucleotide polymorphisms (SNPs) in GABAR subunit genes and to evaluate their contribution to the aetiology of ASD on a sample of Argentinean ASD patients.

**Methods :** A hundred and fifty three ASD patients (86% males) with DSM-IV-TR evaluation and 166 controls (78% males) were studied. Twenty one SNPs located within the GABAR subunit genes were genotyped using DNA sequencing: GABRA4, GABRB3, GABRD and GABRG2. Genetic association to test whether single-locus allele frequencies, genotype frequencies and multilocus haplotype frequencies show differences between cases and controls, as well as Hardy–Weinberg equilibrium (HWE) test for each SNP and pair-wise linkage disequilibrium (LD) estimations were performed using SNPStats and UNPHASED.

**Results:** Both populations were in HWE ($p>0.05$). Significant differences in allele and genotypic frequencies (under dominant model) were observed between groups for SNP rs1912960 in GABRA4. The C allele frequency was significantly increased (OR=1.53, 95%CI: 1.10-2.12, p=0.01) while G allele was significantly decreased (OR=0.65, 95%CI: 0.47-0.90, p=0.01). In the same way, C-C/C-G genotype frequency was significantly increased (OR=1.79, 95%CI: 1.13-2.81, p=0.01) and might confer risk for ASD while G/G genotype was significantly decreased (OR=0.56, 95%CI: 0.35-0.88, p=0.01) and might confer protection. No significant association with ASD was found for the other markers studied for allelic and genotypic frequencies ($p>0.05$). SNPs within genes were in LD ($p<0.05$) and there was no LD between markers across genes studied ($p>0.05$). Haplotype analysis was performed using tagging SNPs within each gene. The combination between markers rs1912960

(GABRA4) and rs211037 (GABRG2) showed a significant association with autism. As a result, two haplotypes were observed: C-T risk haplotype (OR=3.1, 95%CI 1.42-6.8, p=0.001) and G-C protective haplotype (OR=0.71, 95%CI 0.51-0.99, p=0.04). No significant difference between genders was observed (p> 0.05).

**Conclusions:** It has been suggested that α4 subunit might be involved in neuronal hyperexcitability and rs1912960 in GABRA4 has been associated with ASD in different ethnic groups.

Also, the marker rs211037 in GABRG2 was associated with susceptibility to epilepsy and in-silico analysis indicated that this marker plays a role in the transcriptional and splicing regulation.

The frequent co-occurrence of ASD and epilepsy (at least in certain cases) might result from common developmental pathophysiological mechanisms leading to abnormalities in connectivity, imbalance in excitation/inhibition and disrupted synaptic plasticity.

Given that multiple GABAR subunits are blended in varying combinations to form a functional GABA receptor, even minor changes in levels of a particular subunit might modify the make-up of receptors within a particular cell type and alter the GABAergic signalling.

We can conclude that GABRA4 could be involved in the aetiology of autism in the Argentinean dataset both independently and in combination with GABRG2.

**173.046 46** Exploring the Nature of Quantitative Autistic Traits: A Factor Mixture Modeling Approach. R. Grove*[1], A. J. Baillie[1], C. Allison[2], S. Baron-Cohen[2] and R. A. Hoekstra[3], (1)*Macquarie University*, (2)*University of Cambridge*, (3)*The Open University*

Background: Recent research suggests that the social and non-social aspects of autism spectrum conditions (ASC) may have distinct causes at genetic, cognitive and neural levels. This is reflected in the new conceptualisation of autism spectrum disorder outlined in DSM-5, comprising two dimensions of social/communication difficulties and restricted and repetitive behaviours and interests. It has been posited that these core features of ASC can be explained by a deficit in empathising alongside intact or superior systemising. A central debate in the development of DSM-5 across fields of mental health has been whether psychopathology is best conceptualised as a continuum of severity or as discrete categories of disorder. In recent years quantitative measures have been developed assessing autistic traits (Autism Spectrum Quotient, AQ), empathising (Empathy Quotient, EQ) and systemising (Systemising Quotient, SQ) on scales that follow a near continuous distribution. First-degree relatives tend to show intermediate levels of autistic traits, scoring in between clinical and general population groups. It is however unclear whether autistic traits, empathising and systemising are dimensional across study populations and, if so, whether meaningful subgroups can still be identified along these dimensions.

Objectives: To assess whether the latent structure of empathy, systemising and autistic traits is dimensional and whether meaningful subgroups can be identified within this structure.

Methods: Participants included individuals with an ASC (N=363), parents of a child with ASC (N=439) and general population controls (N=232). Participants completed measures of empathy (EQ), systemising (SQ) and autistic traits (AQ) using an online test platform. Factor mixture models were conducted to assess the most parsimonious number of factors and classes that can be identified. Mixture models allow for assessment of both the number of underlying dimensions as well as the identification of classes or groups of individuals. The factors model the severity of the trait, while the latent class variable allows for the classification of subgroups of individuals.

Results: Results highlighted a 2-factor three-class model with one empathising and one systemising factor and three latent classes of individuals. Class 1 was characterised by heightened systemising and low empathy, consisting mostly of individuals with autism and a small proportion of controls. Approximately a third of parents were also represented in the first class. Approximately half the control group and 40% of parents with equivalent empathy and systemising scores were represented in Class 2. Consisting mostly of controls, the third class displayed high empathising and lower systemising scores.

Conclusions: Results suggest three classes of individuals based on levels of empathising, systemising and autistic traits. Class 1 confirms that autism is characterised by impaired empathising alongside intact or superior systemising. The finding that a third of parents were best represented by this class highlights the existence of the broader autism phenotype. Moreover, findings support the notion that autistic traits, as well as empathising and systemising, are continuously distributed across all subpopulations, lending support to a dimensional conceptualisation of autism. This has implications for guiding future conceptualisations of diagnostic criteria as well as the development of assessment instruments and more tailored interventions.

**173.047 47** The Genetic Basis of Autism Spectrum Disorders: Identification and Analysis of Rare Structural Variants in a Family Based Study. N. Brison*[1], W. De La Marche[1], V. De Wolf[1], H. Olivié[2], J. Steyaert[1], I. Noens[3], J. Vermeesch[1], K. Devriendt[1] and H. Peeters[1], (1)*University of Leuven*, (2)*University Hospital Leuven*, (3)*KU Leuven*

Background:

The genetic causes of autism spectrum disorders (ASDs) are heterogeneous and still unknown in the majority of cases. Structural chromosomal variants (or copy number variants (CNVs) were found in sufficiently high frequency to suggest that cytogenetic and microarray analyses are considered in routine clinical workup. An interesting paradigm for clinical practice is that each rare CNV may account for only a small proportion of variance in ASD at the population level but may have a large effect in a few families in which it segregates.

Objectives:

With this study we aim to contribute to the clinical validation of the current knowledge of ASD risk variants and to the identification of novel variants.

Methods:

CNV association studies are performed in a family based cohort. The sample contains 117 families ascertained through one or more autistic probands with normal intelligence or mild intellectual disability. The study cohort contains 519 individuals: 182 probands, 236 parents, 101 unaffected siblings belonging to 117 families. All probands, unaffected siblings and parents are genotyped with high-resolution Illumina Omni2.5-8v1 microarrays. For all individuals, an extensive list of phenotypic information is collected including IQ, SRS scores, 3DI, clinical genetic examination and family history.

Results:

- The number of causal variants found in ASD patients is highly variable between different studies and depends on the inclusion criteria, array resolution and differences in interpretation due to uncertainty on the true etiological role of particular variants. The strength of this study is a prospective family based approach, with extensive phenotyping and genotyping of all family members.
- In 6,7 % of patients with ASD and normal intelligence a variant that contributes to the ASD phenotype was found.
- In sporadic ASD patients more *de novo* ASD susceptibility CNVs were detected whereas in familial cases there were more inherited ASD associated variants. These results suggest that currently known ASD susceptibility loci contribute more in sporadic versus familial ASD.
- For a few cases we showed a different etiology for the ASD phenotype in siblings with a large difference in intelligence (proband with normal intelligence and sibling with moderate intellectual disability).

Conclusions:

We present the results of a family based study on the validity of CNV detection in ASD using a high resolution platform. We study the segregation of known and novel rare CNVs with qualitative and quantitative autism phenotypes. Additionally association studies are performed with respect to amongst others gene content and parental origin.

**173.048 48** Analysis of Differential Methylation in Autism Spectrum Disease Using a Novel Probe-Based Algorithm. T. R. Magalhaes*[1], S. Ennis[2], J. Conroy[3], R. Regan[3] and J. Casey[1], (1)*National Children's Research Centre*, (2)*University College Dublin*, (3)*UCD*

Background:

Hereditary origins for Autism Spectrum Disorder are well established, but other factors are also involved in ASD, as demonstrated by monozygotic twins discordant for autism traits. We studied the role of epigenetics in autism, by comparing methylation profiles of blood samples of 42 ASD samples vs. 108 controls, using the 27K Illumina platform.

Objectives:

To identify probes showing differential methylation in individuals with ASD vs. controls.

Methods:

Methylation studies using the Illumina platform are based on the metric Beta, with states of methylation assigned with sample-based algorithms. We have observed that these approaches assign wrong methylation states to many probes, which led us to develop a probe-based algorithm. We analysed changes in states of methylation/hemi-methylation/unmethylation in ASD samples vs. controls, which we believe is a realistic representation of the underlying biology of the epigenetics of ASD. We have used data mining techniques, such as the PAM clustering algorithm to identify probes with similar profiles. The statistical package R and Python were used in our analysis.

Results:

We have identified 40 probes that show differentially methylation in cases vs. controls, including CpG-islands close to the genes EPHA5, CDK5 and WHSC2. All our samples are of Irish origin; we performed ancestry analysis to validate ancestry was not a counfounding factor in differential methylation. We apply our methodology to a dataset of concordant and discordant ASD twin samples, which is publicly available (Wong, 2013); we observe little overlap between the two datasets, but a few probes show similar methylation profiles.

Conclusions:

We observe differential methylation for 40 probes in a cohort of 42 Irish individuals with ASD. Some of the probes are close to genes that might have a role in ASD, such as the axon guidance gene EPHA5. Our study suggests a role for epigenetics in ASD.

**173.049 49** Assessment of Sources of Methylation Variation and Their Relationship to Autism Spectrum. M. D. Fallin*[1], S. V. Andrews[2], B. K. Lee[3], C. J. Newschaffer[3], G. C. Windham[4], L. A. Schieve[5], L. A. Croen[6], A. P. Feinberg[2] and C. Ladd-Acosta[2], (1)*Johns Hopkins School of Public Health*, (2)*Johns Hopkins University*, (3)*Drexel University School of Public Health*, (4)*California Dept of Public Health*, (5)*Centers for Disease Control and Prevention*, (6)*Kaiser Permanente Northern California*

Background: Understanding DNA methylation variance in the context of autism spectrum disorders (ASD) may improve our understanding of the underlying molecular architecture involved in the etiology of ASD. The Study to Explore Early Development (SEED) is a multisite population-based case-control study of children aged 2-5 years with ASD and two control groups, one drawn from the general population and one with non-ASD developmental problems. We chose to examine DNA methylation among children in SEED because it is one of the only epidemiologic studies of ASD with comprehensive phenotypic evaluation, broad prenatal environmental exposure information, genome-wide genotyping data, and whole blood available for epigenomic measurements, all from the same individuals.

Objectives: The goal of this study is to define sites of variable DNA methylation in our SEED methylation dataset, identify biological sources of methylation variation, and determine their relationship to ASD.

Methods: Among 611 children enrolled in SEED, we generated unified genome-wide genotype data using the Illumina HumanOmni1-Quad BeadChip and genome-scale DNA methylation data using the 450K. Rigorous quality control measures were applied to the genotyping and methylation datasets resulting in a total of 593 children with more than 800,000 measured genotypes and over 485,000 methylation measurements. We identified genomic loci exhibiting variable methylation across the 593 SEED individuals. We then determined the relationship between the variably methylated sites and particular features of the genome sequence, and their association with ASD.

Results: Among the 450K probes exhibiting variable methylation between subjects, we identified 83,265 probes with a particular variation in methylation signal, defined herein as "gap probes", which cluster into 2 or 3 distinct

groups separated by a "gap" in methylation values. We are in the process of characterizing the source of this gap probe behavior and determining whether the gap behavior is phenotypically driven, i.e. result from case or exposure status, and how genetic sequence contributes to this. We have already determined that a large fraction of these gap probes (25,427 or 30.1%) are at least in part attributed to the presence of a single nucleotide polymorphism (SNP) at the interrogated CpG site, at the single-base extension, or in the probe itself. It is possible that these methylation-associated SNPs and/or their associated haplotypes differ between ASD cases and controls. Therefore, we have begun to discern the role of SNPs (through identification of methylation quantitative trait loci, or meQTLs) and copy number variants in the genetic contribution to the gap probe methylation pattern. Because we have genome-wide genotype and genome-scale methylation data from the same SEED children, we can directly evaluate our SNP-methylation findings in relation to ASD status. The relationships we identify will be presented at the meeting.

Conclusions: We have identified thousands of variably methylated positions that appear to be related to underlying features of the genomic sequence. Relating these to ASD status may provide valuable new insights into the etiology of disease.

**173.050 50** AutDB: A Modular Database for Accelerating Autism Genetic Research. E. Larsen*, U. Kuppuswamy and S. B. Basu, *MindSpec, Inc.*

Background: A major focus of research in the post-genomic era is to decipher the heterogeneous genetic landscape underlying the pathogenesis of complex human diseases such as Autism Spectrum Disorders (ASD). A number of genes in which rare and/or common genetic variants thought to potentially play a role in ASD onset and pathogenesis have been identified. The advent of new techniques such as next generation sequencing (NGS) has resulted in a significant increase in the number of ASD genes with rare genetic variants. With the accelerated growth of genetic data obtained from ASD individuals adding to the already complex genetic landscape of this disease, there is a critical need for databases specialized in the storage and assessment of this data.

Objectives: The autism genetic database AutDB (http://autism.mindspec.org/autdb/Welcome.do) was developed to serve as a publically available web-based modular database for the on-going curation and visualization of ASD candidate genes. Since its release in 2007, AutDB has been become widely used by individual laboratories in the ASD research community, as well as by consortiums such as the Simons Foundation, which licenses it as SFARI Gene. AutDB has been designed using a systems biology approach, integrating genetic information within the original Human Gene module to corresponding data in subsequent Animal Model, Protein Interaction (PIN) and Copy Number Variant (CNV) modules. We had previously performed functional profiling of a reference dataset of ASD-associated genes (Kumar et al., PLoS One 2011) and decided to utilize an updated reference dataset of candidate genes to identify potentially novel enriched molecular functions and pathways.

Methods: ASD candidate genes are systemically extracted from peer-reviewed primary scientific literature and manually curated for inclusion in AutDB. A subset of annotated genes with at least suggestive evidence for a role in ASD was selected for further use in functional profiling analyses.

Results: The number of ASD susceptibility genes in the Human Gene Module of AutDB has increased from 304 genes in December 2011 to 573 genes in September 2013, which demonstrates both the continued discovery of ASD candidate genes and the ongoing curation of these genes into AutDB. In addition, the usage of NGS techniques has contributed to a dramatic increase in the number of rare variants identified in ASD candidate genes (from 1202 in Dec 2011 to 3399 in September 2013) compared to common variants (from 534 to 812 over the same period). Functional profiling using a subset of annotated ASD-linked genes provides insight into the enriched molecular functions of these genes, including gated ion channel activity, synaptic transmission, axon guidance, and chromatin binding.

Conclusions: AutDB serves as a valuable resource for understanding the ever-evolving genetic landscape of ASD and provides researchers with information useful in bioinformatics analyses such as those described above that will aid in

unraveling the molecular mechanisms underlying the disease.

**173.051 51** Blood-Brain DNA Methylation Concordance in Autism Spectrum Disorders. S. V. Andrews*[1], L. A. Croen[2], L. A. Schieve[3], K. D. Hansen[1], B. K. Lee[4], C. J. Newschaffer[4], A. P. Feinberg[1], C. Ladd-Acosta[1] and M. D. Fallin[5], (1)*Johns Hopkins University*, (2)*Kaiser Permanente Northern California*, (3)*Centers for Disease Control and Prevention*, (4)*Drexel University School of Public Health*, (5)*Johns Hopkins Bloomberg School of Public Health*

Background: Epigenetic processes in the brain have been investigated for their potential implications in many neurological disorders, because of the important role of epigenetics in brain function and development. While many useful epigenetic signatures have been discovered in the brain for numerous disorders, such as Alzheimer and Parkinson diseases, and autism spectrum disorders (ASD), an obvious limitation is the inability to test for them pre-mortem.

Objectives: The purpose of this work is to identify the extent to which a more easily-accessible tissue, such as blood, can be used as an indicator of epigenetic signatures for ASD that have been discovered in the brain.

Methods: Ladd-Acosta et al. found four regions of the genome to be differentially methylated between ASD cases and controls in a cohort of 41 post-mortem brain tissue samples. We will attempt to replicate these regions using methylation measurements in whole-blood derived DNA from 609 individuals, including 292 ASD cases and 317 controls, enrolled in the Study to Explore Early Development (SEED), a multisite population-based case-control study of children aged 2-5 years with ASD and a control group drawn from the general population.

Results: We will present results detailing the extent to which differentially methylated regions discovered in the brain samples are replicated in the SEED cohort.

Conclusions: The utility of replication in this context would be to provide additional evidence for the methylation differences identified in these regions, and to inform the development of non-invasive biomarkers for both ASD and ASD-related exposures.

**173.052 52** Common Polygenic Variations in Autism. J. Carayol[1], B. Génin[1], C. Amiet[2], F. Liebaert*[1], R. Thiébaut[1], B. Abrahams[3] and T. W. Frazier[4], (1)*IntegraGen*, (2)*GHU Pitié-Salpêtrière, APHP*, (3)*Albert Einstein College of Medicine*, (4)*Cleveland Clinic*

Background:

Autism Spectrum Disorder (ASD) has a strong genetic component. The inheritance pattern of ASD in most families is complex and caused by multiple genetic and environmental factors. While rare and de novo genetic variation are known to affect liability, a recent study suggests that common genetic polymorphisms exert substantial additive genetic effect on ASD liability and could explain up to 40% of genetic variance of autism in simplex families and 60% in multiplex families.

Objectives:

To better characterize the common genetic background of multiplex and simplex autism and identify an optimal set of single nucleotide polymorphisms (SNPs) that could discriminates affected from non-affected individuals when combined in a polygenic model.

Methods:

A genome-wide association study based on 1,490 children with autism from the Autism Genetic Resource Exchange (AGRE) and the Simons Simplex Collection (SSC) and 1,335 independent controls (Discovery sample) was performed. Genetic risk scores (GSs) were computed from SNPs selected according to varying liberal P-values criteria and evaluated in an independent Validation sample of 452 affected children from the Autism Genome Project (AGP), including multiplex and simplex families and 1,144 independent controls. Using a principal component analysis, we limited the two samples to individuals with a homogeneous European genetic background to avoid any confounding effects. For statistical power consideration, all cases were required to be diagnosed with an autistic disorder. In the Validation sample we explored which SNPs jointly explained most of the genetic variance in multiplex and simplex autism based on P-value criteria and consistent direction of SNP's allele effect. New GSs were evaluated in an independent Replication sample combining 554 affected individuals without sibling history of ASD from the AGRE, SSC and AGP collections, excluded from previous analysis because of a heterogeneous European genetic background and 1,986 controls.

Results:

The GSs computed in the Discovery sample were significantly associated with autistic disorder and explained up to 6% of the genetic variance in the Validation sample. Exploratory analyses in the Validation sample determined that a subset of 5,284 SNPs could explain up to 24% and 28% of genetic variance in simplex and multiplex autism. Consistency of risk allele between the Discovery and the Validation sample stratified according to multiplex/simplex information was observed for 2,061 SNPs. Because of different genotyping technology, only 1,706 SNPs were available for analysis in the Replication sample. The corresponding GS was significantly associated to autistic disorder ($P=1.4x10^{-169}$) and explained up to 24% of genetic variance with an estimated 0.82 area under the curve (AUC). Assuming a pre-test risk of 24.8% for children with developmental delays, a GS based on 1,706 SNPs identified children with up to 50% and 72% risk of autism.

Conclusions:

This study provides further evidence for a common polygenic component in autism and a common genetic background between simplex and multiplex autism. Based on these results, we show that a combination of multiple risk-associated common variants in a GS may have the ability to identify children with a higher risk of autism.

**173.053 53** Common Polymorphisms in GABRB3 Are Associated with Asperger Syndrome and Related Endophenotypes.

V. Warrier*[1], S. Baron-Cohen[2] and B. Chakrabarti[3], (1)*University of Cambridge*, (2)*Cambridgeshire and Peterborough NHS Foundation Trust*, (3)*University of Reading*

**Background:** Autism Spectrum Conditions (ASC) are neurodevelopmental and are associated with deficits in social interaction and communication alongside unusually repetitive, restricted, and stereotyped behaviour. Within the spectrum there is considerable variability in both cognitive and behavioural endophenotypes. Asperger Syndrome (AS) is a subset of ASC where the development of language and intelligence is preserved. Genetic association and expression studies have consistently implicated the GABA-ergic system in ASC. *GABRB3* encodes a key component of the GABA-ergic system and has been previously associated with ASC and normative variation in empathy and sensory sensitivity. Few genetic studies have focused specifically on AS.

**Objectives:** To conduct a candidate gene association study of common polymorphisms in *GABRB3* for AS and six other related endophenotypes.

**Methods:** 45 single nucleotide polymorphisms (SNPs) were tested for association with AS in a cohort of n = 530 individuals (412 controls: 185 males, 227 females; 118 cases: 74 males, 44 females). Additionally, we also tested the 45 SNPs for association with six related quantitative traits measured in controls through the following tests: the Empathy Quotient (EQ), the Autism Spectrum Quotient (AQ), the Systemizing Quotient-Revised (SQ-R), the Embedded Figures Test (EFT), the Reading the Mind in the Eyes Test (RMET), and the Mental Rotation Test (MRT). Allelic and two-loci SNP-SNP interaction tests were performed for both case-control and quantitative traits. Additionally 2-loci, 3-loci, 4-loci and one 7-loci haplotype analyses were performed in the AS case-control sample. All analyses were performed using Plink version 1.07. Correction for multiple testing for allelic association and SNP-SNP interaction tests were performed using Bonferroni correction, after accounting for LD between the SNPs investigated. Haplotype analyses were corrected using permutation correction.

**Results:** Three individual SNPs (rs7180158, rs7165604, rs12593579) were significantly associated with a clinical diagnosis of AS. Using haplotype analysis, we identified a 19kb genomic region (rs7180158-rs7174437; Chr15:26978238 - 26997923) that formed an LD block, which was significantly associated with AS. This genomic region encompasses all three significantly associated SNPs with AS and is less than 10kb downstream from 155CA-2, a microsatellite marker that was previously associated with ASC.

Two SNPs (rs9806546, rs11636966) were significantly associated with EQ in controls. We did not identify any allelic associations with the remaining quantitative endophenotypes tested. Two SNP-SNP pairs – rs12438141-rs1035751, rs12438141-rs7179514 – showed significant interaction in association with the EFT in controls. One SNP-SNP pair – rs7174437-rs1863455 – was significantly associated with the MRT in controls.

**Conclusions:** This is the first study to specifically test this number of common SNPs in GABRB3 with AS, and with a comprehensive set of

endophenotypes. The current study confirms the role of *GABRB3* as an important candidate gene in both ASC and normative variation in related endophenotypes.

**173.054 54** Concordance in Symptom Severity and Face Processing Among Twins with and without Autism. E. E. Neuhaus*, S. J. Webb, R. Bernier, A. Kresse and S. Faja, *University of Washington*

Background: Autism spectrum disorder (ASD) stems in part from heritable and genetic factors, as evidenced by higher rates of ASD concordance among monozygotic (MZ) twins relative to dizygotic (DZ) twins. Although the precise mechanisms underlying these factors are not fully understood, behavioral and electrophysiological markers of social functioning and social cognition provide avenues through which to explore patterns of genetic influence. Within social cognition, the area of face processing is of particular relevance to ASD. Not only are face-processing impairments well documented in ASD, but recent evidence supports a genetic contribution to face-processing among typically developing individuals.

Objectives: Our goals in this study were to examine concordance within twin pairs on measures of (1) diagnostic severity as indices of social functioning; (2) memory for faces as an index of social cognition; and (3) electrophysiological response to faces as an index of brain response to social stimuli. Stronger correspondence between twins within MZ pairs relative to DZ pairs would provide support for genetic contributions to these domains.

Methods: Within a larger sample, we identified 27 MZ and 19 DZ twin pairs across two diagnostic groups: concordant for the presence of an ASD (n=19) and concordant for the absence of an ASD (n=27). Twins ranged in age from 5 years to 22 years (mean = 11.1 years) and included both male (n=59) and female participants (n=33). Over the course of multiple visits, twins completed measures of diagnostic status (ADOS, ADI-R), intellectual functioning (WASI), social cognition (memory for human faces), and electrophysiological response to faces.

Results: Behavioral findings suggest intriguing patterns of correspondence within twin pairs across these measures. Severity of ASD symptoms as assessed with the ADOS calibrated severity score was correlated within MZ twin pairs but not within DZ pairs. However, this pattern was reversed for symptom severity assessed via parent report on the ADI-R, for which DZ pairs were more strongly correlated than MZ pairs. With regard to social cognition, DZ twins showed more evidence of correspondence within pairs than did MZ twins, although correspondence in both groups was enhanced when controlling for intellectual functioning. Analysis of associated electrophysiological markers is currently underway. We anticipate that markers relevant to the processing of human faces (e.g., P100, N170) will be more highly correlated within MZ twin pairs than within DZ pairs. We also predict that correlations between behavioral and electrophysiological measures will be stronger among participants without ASD than among those with ASD.

Conclusions: These findings highlight the potential contribution of genetic factors to social functioning and social cognition among individuals with ASD, but imply that these influences are not straightforward. Whereas MZ twin pairs showed greater similarity than DZ twins on some measures, other measures revealed greater similarity within DZ twins. This pattern suggests nuanced and complex genetic mechanisms for social and cognitive development.

**173.055 55** Cross-Disorder CNV Interactome. R. Corominas*[1], G. N. Lin[1], X. Yang[2], D. E. Hill[3], M. Vidal[3] and L. M. Iakoucheva[1], (1)*University of California San Diego*, (2)*Dana-Farber Cancer Institute*, (3)*Harvard Medical School*

Background: Neuropsychiatric disorders such as autism, schizophrenia, bipolar disorder and intellectual disability are major burden to society. Our current knowledge of their underlying pathophysiology remains limited. However, a contribution of genetic factors has been clearly demonstrated. It is now firmly established that rare Copy Number Variants (CNVs) play significant role in the risk of psychiatric disorders. Interestingly, many high-risk rare CNVs cross disorder boundaries and are implicated in several psychiatric disorders.

Objectives: To advance our understanding of CNV contribution to psychiatric diseases, we are investigating how the genes from high risk CNVs interact on a protein level. We are testing the hypothesis that cross-disorder CNVs have common and unique interacting protein partners

by building and analyzing a cross-disorder protein-protein interaction (PPI) network.

Methods: We have selected 11 high risk CNVs (containing 169 genes) that are firmly implicated in two or more psychiatric disorders for this study. First, a library of 169 open reading frame (ORF) clones corresponding to cross-disorder CNV genes will be assembled from human ORFeome collection and from our in house clone library. For the cases when the clone is not available, we will clone the gene using commercially available total purified human brain RNA. Then, we will experimentally identify interacting partners for these 169 CNV genes using high-throughput yeast-two-hybrid system. The clones will be screened against the whole human ORFeome 9 (169x17,000 genes) to identify new partners, and against themselves (169x169) to identify directly interacting CNV genes. Finally, we will build and analyze the cross-disorder CNV interactome.

Results: We extracted binary physical PPIs reported for these 169 genes from the public databases and from our recent studies of autism and schizophrenia and observed that 33% of these genes do not have any interaction data available; and only 3.5% of them interact with each other. Furthermore, when the genes with PPIs are merged into the CNV nodes, only 3 CNVs become connected via literature curated interactions (3q29, 7q11.23, 22q11.21), and an additional 5 CNV become connected by the PPIs from our recent studies (1q21, 17q12, 15q11.2, 16p13.11 and 16p11.2). In total, only a small proportion of CNV genes (13/169 or 7.7%) are found to be directly interacting at the protein level. This is likely due to the fact that they have not been tested for interactions with other CNV genes. We are filling this knowledge gap by performing the screens described in the methods section above.

Conclusions: We are building the protein network connecting genes from high risk copy number variants implicated in four psychiatric disorders. This network will identify sets of protein partners that are common and unique to these disorders. This knowledge will help to expand our understanding of the molecular basis of psychiatric disorders.

**173.056 56** Defining the Clinical Phenotype of Recurrent Copy Number Variation at Chromosome 1q21.1. R. Bernier*[1], B. Reilly[2], E. Hanson[3], R. P. Goin-Kochel[4], L. Green-Snyder[3], J. Tjernagel[5], J. Gerdts[1], A. Stevens[1], W. A. Faucett[6], E. H. Sherr[7], C. L. Martin[6], D. H. Ledbetter[6], J. E. Spiro[5] and W. Chung[8], (1)*University of Washington*, (2)*Lakeside Center for Autism*, (3)*Boston Children's Hospital*, (4)*Baylor College of Medicine*, (5)*Simons Foundation*, (6)*Geisinger Health System*, (7)*University of California, San Francisco*, (8)*Columbia University Medical Center*

Background: Copy number variation (CNV) at chromosomal region 1q21.1 is associated with a range of phenotypes, including autism spectrum disorder (Mefford et al, 2008; Girirajan et al, 2013). Given the variability of the phenotype, the limited sample sizes of previous studies, and the lack of comparison cohorts with which to more precisely refine the behavioral phenotype, characterization of the phenotype and commonly associated features are needed for deletions and duplications at 1q21.1.

Objectives: To describe the psychiatric and behavioral phenotype of 1q21.1 deletion and duplications and identify shared and distinct features of between deletions and duplications carriers.

Methods: Participants included 36 individuals (19 children) with a confirmed 1q21.1 deletion or duplication (19 deletion; 17 duplication) ascertained through the Simons VIP connect online portal. Detailed medical history was collected through interview and medical records review. Standardized diagnostic and detailed neuropsychologic assessment was conducted at one of three participating Simons VIP clinical sites and included ADOS and ADI, as well as cognitive, language, behavioral and adaptive skills assessment. Multivariate ANOVA was used to examine differences in phenotypic presentation of individuals with deletions and duplications.

Results: Of the 19 deletion patients, 9 were children. Of the 17 duplication patients, 10 were children. All but one of the children was the initially identified patient. In the deletion cohort anxiety/mood disorders (31%), developmental coordination disorder (19%), ASD (12%) and intellectual disability (12%), were the most common psychiatric disorders. In the duplication cohort, the most common diagnoses were ASD (44%), ADHD (31%), intellectual disability (31%), and developmental coordination disorder (25%). Deletion carriers generally reported a higher frequency of some medical manifestations than duplications carriers: cataracts (17% vs 0%),

seizures (17% vs 0%), short stature (25% vs 0%), hypothyroidism (17% vs 0%), genito-urinary problems (17% vs 9%), and microcephaly (34% vs 0%). Similar frequencies of hypotonia (58% vs 54%) and lower rates of macrocephaly (0% vs 27%) and congenital heart disease (0% vs 18%) were reported in deletions relative to duplications. For deletions and duplications, the children were more impaired than the adults in cognitive ability, adaptive functioning, and parent report of ASD symptoms. For adults average nonverbal IQ, verbal IQ, adaptive functioning, and ASD symptomatology were in the normal range, while for children nonverbal IQ, verbal IQ, and adaptive ability fell in the borderline low normal range and ASD symptomatology fell in the clinical ASD range. In both adults and children, deletion carriers did not significantly differ from duplication carriers in cognitive and adaptive ability or ASD symptom severity. When only the initially identified probands were compared, there were no differences between deletion and duplication carriers in cognitive and adaptive functioning, but duplication carriers showed significantly greater ASD symptom severity (ADOS CSS $F(1,14)=6.3$, $p=.02$).

Conclusions: Psychiatric and other medical disorders were common in both individuals with the 1q21.1 deletion and duplication. While deletion and duplication carriers shared some nonspecific traits (e.g. borderline cognitive functioning), there was a high and increased frequency of ASD in 44% of duplication carriers relative to 12% of deletion carriers.

**173.057 57** Differentially Expressed Small Non-Coding RNA in the Temporal Cortex of the Autism Brain. B. P. Ander*, N. Barger, B. Stamova, F. R. Sharp and C. M. Schumann, *UC Davis MIND Institute*

Background: The superior temporal sulcus (STS) plays a critical role in social behavior, a core impairment in autism, yet the molecular mechanisms that underlie abnormal STS function remain largely unexplored. Small non-coding RNAs (sncRNA), including microRNA (miRNA) and small nucleolar RNA (snoRNA), show increased importance as key regulators of translation during development and throughout life. Aberrant expression of sncRNA could lead to widespread changes in protein and cellular function related to autism. This study evaluated differences is sncRNA expression in the STS in the autism brain. In addition, this study sought to determine if differences were localized to association cortices, such as STS, or may also include neural regions involved in more basic perceptual processing, such as the primary auditory cortex (PAC), that are not typically associated with the core impairments of autism.

Objectives: Examine the changes in expression of small non-coding RNAs expressed in association (STS) and primary (PAC) cortex of autism and typically developing brains.

Methods: Brain tissue from subjects diagnosed with autism (n=10) and typically developing controls (n=8) was obtained from the Harvard Brain Tissue Resource Center. The STS and PAC were dissected from each fresh-frozen brain. Total RNA was isolated from each region and assessed for concentration and quality. Two hundred nanograms of total RNA were processed on Affymetrix GeneChip miRNA 3.0 Arrays. Arrays were scanned and resulting CEL files analyzed with Partek Genomics Suite. Only small non-coding RNAs (mature miRNA, precursor miRNA and snoRNA) with human annotation (5663 targets) were included in the analysis. Functional significance of altered miRNA was determined through analysis of over-representation of their computationally derived mRNA targets in KEGG pathways using DIANA miRPath and Exploratory Gene Association Networks (EGAN) software.

Results: In STS, the expression of 3 miRNA significantly differed ($P<0.005$, $FC>|1.2|$) between autism and typically developing control brains (miR-1, miR-4753-5p, and miR-513a-5p). These miRNA regulate pathways relating to synapse, brain maturation function and processes, and immune function. An additional 11 stem-loop precursor miRNA and 6 snoRNA were also different in STS. In PAC, 3 miRNA were significantly different in autism compared to typical control (miR-297, miR-664, and miR-4709-3p). These were unique to PAC and may represent affected function of other cell signaling pathways and developmental cues. There were also 7 stem-loop precursor miRNA and 4 snoRNA differentially expressed in PAC. Commonly affected elements/functions of miRNA in both regions, include Akt and glutamate signalling. The presence of significantly altered snoRNA in autism brain may implicate alterations in splicing mechanisms and patterns as important contributors to autism.

Conclusions: Regional differences in miRNA and other sncRNA expression were observed between autism and control brains in the STS and PAC. These changes in small regulatory non-coding RNA may have important regulatory effects on mRNA transcript splicing and translation to proteins. These findings help identify molecular mechanisms underlying autism and elucidate specific targets to restore perturbations that might occur in autism.

**173.058 58** Early Intervention in Autism: Wide-Locus GWAS Leading to Novel Treatment Options. K. M. Wittkowski*[1], B. Bigio[1], V. Sonakya[1], M. K. Tonn[2], F. Shic[3], M. Ascano[1], C. Nasca[1] and G. Gold-Von Simson[4], (1)*The Rockefeller University*, (2)*Hochschule Koblenz*, (3)*Yale University School of Medicine*, (4)*New York University*

Background:

The prevalence of autism spectrum disorders (ASD) has increased 20-fold over the past 50 years to >1% of U.S. children. Although twin studies attest to a high degree of heritability, the genetic risk factors are still poorly understood.

Objectives:

From recent results in a comorbid disease, childhood absence epilepsy, we had hypothesized that axonal guidance and calcium signaling are involved in autism as well. Our study aimed at identifying overlapping genetic risk factors for both neurodevelopmental diseases as well as indications for differences in the etiology to guide with developing novel autism-specific pharmacological interventions.

Methods:

We analyzed data from the two stages of the Autism Genome Projects as independent populations using u-statistics for genetically structuredwide-locus data and added data from unrelated controls to explore epistasis. To account for systematic, but disease-unrelated differences in (non-randomized) genome-wide association studies (GWAS) and for conducting multiple tests in overlapping genetic regions, we present a novel study-specific criterion for 'genome-wide significance'.

Results:

Enrichment of the results in both studies with related genes confirms this hypothesis. Additional ASD-specific variations identified in this study suggest protracted growth factor signaling as causing more severe forms of ASD. Another cluster of related genes suggests a novel class of ion channels as additional, ASD-specific drug targets. The involvement of growth factors suggests the time of accelerated neuronal growth and pruning at 9–24 months of age as the period where treatment with a novel class of ion channel modulators would be most effective in preventing progression to more severe forms of autism.

Conclusions:

These results are the first to suggest a pharmacological intervation in autism based directly on observations in patients with autism. The major difference for this novel approach to identify ASD-specific risk factors and drug targets and previous statistical approaches is that genetic risk factors are assumed to be epistatic (within several neighboring SNPs) and in linkage disequilibrium with more than a single SNP. By extension, the same computational biostatistics approach could yield profound insights into the etiology of many common diseases from the genetic data collected over the last decade.

**173.060 60** Examining the Overlap of Autism Spectrum Disorder and 22Q11 Deletion Syndrome Using Standardized Clinical Assessments. N. Evans*[1], S. Fernandez-Carriba[1], E. L. Smearman[2], K. Rockers[2], K. Coleman[3], J. F. Cubells[4] and O. Ousley[2], (1)*Marcus Autism Center, Children's Healthcare of Atlanta and Emory University School of Medicine*, (2)*Emory University School of Medicine*, (3)*Nell Hodgson Woodruff School of Nursing at Emory University*, (4)*The Emory Autism Center*

Background:

In order to better understand the biological causes of autism spectrum disorder (ASD), researchers have attempted to identify known genetic syndromes that may overlap with ASD. While some studies find that ASD does not co-occur with 22q11 deletion syndrome (22q11DS), others have found that between 15 and 50 percent of individuals with 22q11DS also have ASD.

Objectives:

Our study aimed to provide a conservative estimate of the occurrence of ASD among a cohort of children (ages 6-12) and adolescents/adults

(ages 14-29) with 22q11DS, using rigorous, research-based diagnostic procedures.

Methods:

This study evaluated 56 participants between the ages of 6 to 29 with 22q11DS for ASD. We divided the total group into two cohorts, children (*n* = 23) ages 6 to 12 (*M* = 9.64, 48% female) and adults (*n* = 33) ages 14 to 29 (*M* = 19.60, 56% female). The *Autism Diagnostic Interview-Revised (ADI-R)* and *Autism Diagnostic Observation Schedule (ADOS)* were administered and, along with clinician best estimate diagnosis, informed ASD designation. Following the Collaborative Programs of Excellence in Autism (CPEA), we identified individuals as having autism, Asperger's disorder, or pervasive developmental disorder – not otherwise specified (PDD-NOS) using a hierarchical algorithm.

Results:

Based on the ADOS, 41.1% of the participants' scores met the cutoff for an ASD. When using the ADI-R, 37.5% met the cutoff for an ASD. We found that of our 56 participants, 10 (17.9%) met both the ADI-R and ADOS, and also received clinician's best estimate of diagnosis as ASD; that is, they met CPEA criteria for an ASD. More than a third of participants (39.3%, n = 22) met neither the ADI-R nor ADOS cut-offs. In addition, ASD-related problems were evident in those who did not meet overall ASD diagnostic thresholds. In particular, 37.5% met the ADI-R cutoff for the social domain, 32.1% for the communication domain, and 46.4% for the repetitive behavior domain. ADI-R results indicate that more than half of our participants (66.1%, n = 37) met at least one of the social, communication, or repetitive behavior domain cut-offs (ADI-R sub domains A-C).

Conclusions:

The data support the conclusion that strictly defined ASDs do occur within the 22q11DS population. Knowledge of this association should lead to 1) earlier diagnosis of ASDs in individuals with 22q11DS and 2) targeted interventions and therapies, such as pharmacological and behavioral approaches (Vorstman, 2006). Awareness of this association may also lead to specific hypotheses regarding the etiology of ASD (Karam et al., 2010; Grayton et al., 2012). Thus, we recommend that all individuals with 22q11DS be screened for ASD as a part of their standard clinical care. Results will be discussed in regards to DSM 5 diagnoses of autism spectrum disorder and social (pragmatic) communication disorder.

**173.061 61** Heterogeneity in 5-Httlpr Genotype-Phenotype Effects.

E. H. Cook*[1], E. Kistner-Griffin[2], S. Jacob[3], F. Najjar[1], S. J. Guter[1], N. J. Cox[4] and J. S. Sutcliffe[5], (1)*University of Illinois at Chicago*, (2)*Medical University of South Carolina*, (3)*University of Minnesota*, (4)*University of Chicago*, (5)*Vanderbilt University*

Background:

Initially, overtransmission of the low-expressing short (S) allele of the 5-HTTLPR to probands with autism from their parents was found. Subsequently, the most complete meta-analysis [PMID 16103890] provided replication of this finding but more importantly provided statistical support for the heterogeneity across studies. Subsequent studies have examined potential sources of heterogeneity, including potential relationship to phenotype [PMID 17151167] with an indication that the "protective" allele for ASD, the higher expressing long (L) allele may be a risk allele for aspects of restricted and repetitive behaviors. More recently, evidence has been provided that a SNP (rs25531) within the 5HTTLPR leads to a reclassification of long alleles into high expressing (La) and lower expressing (Lg).

Objectives: To determine if the low expressing alleles (S and Lg) are overtransmitted to subjects with ASD.

To determine if the high expressing allele (La) is associated with higher scores on the Restricted and Repetitive Behavior-Revised Compulsions/Rituals/Insistence on Sameness factor (RBS-R CRS).

Methods:

The study was conducted as part of Project I of the IRB approved study, "Autism Center of Excellence: Translational Studies of Insistence on Sameness in Autism." Subjects ranging in age from 3.16-44.3 years met ADI-R and ADOS criteria on both instruments for either autism or autism spectrum disorder. They had clinical confirmation of an ASD by both a psychologist and

a child and adolescent psychiatrist. Genotyping was performed by PCR amplification and capillary electrophoresis sizing as previously reported [PMID: 11920155] with an additional restriction digest with MspI to genotype rs25531. Genotyping occurred after collection of phenotype measures and was blind to all phenotype measures. Genetic analysis was performed using FBAT for affection (transmission to ASD probands) and the quantitative phenotype RBS-R CRS as the primary quantitative trait hypothesis. Age and sex were tested for association with quantitative phenotypes and were adjusted for when $p<0.10$.

Results: No Mendelian errors were identified for 5-HTTLPR and the data were consistent with HWE ($p=0.54$). FBAT revealed overtransmission of the low-expressing alleles (S and Lg) to those affected with ASD (all ancestry groups combined: 153 complete nuclear families, S-E(S) ;14.5, Var(S) 14.5, z 2.29, $p = 0.022$; European ancestry (EA): 107 complete nuclear families, S-E(S) 11, Var(S) 29.5, z 2.025, $p = 0.043$). In contrast, RBS-R CRS scores were higher when the La allele was transmitted (all ancestry groups combined: 150 complete nuclear families, S-E(S) ;147.85, Var(S) 4361.70, z 2.24, $p = 0.025$; EA: 105 complete nuclear families, S-E(S) 150.485, Var(S) 2893.819, z 2.78, $p = 0.005$).

Conclusions:

The study found a pattern which may partially account for the heterogeneity of studies of 5-HTTLPR. We found overtransmission of the low-expressing S and Lg alleles to probands with ASD yet found that the high expressing La allele was associated with higher compulsion, ritual and insistence on sameness factor scores. This paradox may account for heterogeneous results in samples that differ in severity of CRS symptoms.

**173.062 62** Maternally Acting Gene Alleles (MAGAs) in Autism: A Meta-Analysis of Two GWAS Study Results. W. G. Johnson*[1], E. Stenroos[2] and S. Buyske[3], (1)*Rutgers University - Robert Wood Johnson Medical School*, (2)*Rutgers University - Robert Wood Johnson Medial School*, (3)*Rutgers University*

Background: Maternally Acting Gene Alleles (MAGAs) act in maternal tissues prenatally to alter fetal environment and affect offspring phenotype, independently of whether or not they are inherited by the fetus. At least 70 MAGAs are known to date, mostly in neurodevelopmental disorders. From the mother's perspective, MAGAs are genetic factors, producing proteins and perhaps microRNAs or circular RNAs. From the fetus' perspective, MAGAs are environmental factors. We previously carried out the first two maternal analyses of GWAS data for MAGAs using two autism datasets, the AGRE dataset and later the AGP dataset. We found genome-wide significant peaks in regions of chromosomes 1 and 3.

Objectives: Here, we carried out a meta-analysis of these two results to identify and characterize additional regions of interest.

Methods: We used the Weinberg log-linear method through a convenient implementation in EMIM. Study-specific results for the two datasets were then meta-analyzed.

Results: In the AGRE dataset, we identified 9 regions of interest; in the AGP dataset we identified 5 regions of interest. In the meta-analysis, we identified 5 new regions of interest. Thus, we have found 19 regions of interest so far, all of maternal origin. Three of these regions contained numerous SNPs in high LD with low p-values. Three of the SNPs with probes with high degrees of Y-homology need to be confirmed with more stringent methods. Two of the regions had been previously implicated in autism, i.e. *SHANK2* and *CNTN5.*

Conclusions: We have now identified 19 regions of interest for MAGAs in autism. We will now study them further by analysis of other datasets and by re-genotyping with more stringent methods and by and imputation. These studies could lead to identification of DNA variation in these regions whose action may contribute to autism. We hope these studies will lead to better understanding of the pathogenesis of autism, to approaches to identifying risk of autism prenatally or even before the onset of pregnancy, and perhaps to methods of preventing or treating autism at a very early stage.

## 174 Medical and Psychiatric Co-Morbidity

**174.063 63** Mediators Between Autistic Traits and Anxiety Symptoms in Young Adults: ARE There Specific Mediators for Different Anxiety Subtypes? S. M. Liew*, N. G. Thevaraja, R. Y. Hong and I. Magiati, *National University of Singapore*

**Background:** The positive association between anxiety and Autistic Spectrum Disorders (ASD), as well as autistic traits, has been well documented. However, less is known about whether - and

which- social, communication or behavioral factors mediate this relationship. In addition, it is not known whether there may be specific mediators between autistic traits and certain anxiety subtypes or symptoms (i.e. social, generalized or obsessive-compulsive anxiety symptoms).

**Objectives:** This study extended earlier work by Rosbrook and Whittingham (2010) and attempted to validate parts of the theoretical model of anxiety in ASD proposed by Wood and Gadow (2010). Specifically, the role of five potential mediators (social problem-solving, teasing experiences, social competence, prevention from/punishment for preferred repetitive behaviors, and frequent aversive sensory experiences in daily life) in the relationship between autistic traits and anxiety symptoms was investigated in an undergraduate Singaporean student sample. Furthermore, this study explored whether some of these mediators were specific to certain types of anxiety symptoms only (i.e. social, generalized or obsessive-compulsive).

**Methods:** Taking a dimensional approach to understanding autistic traits, 252 undergraduate university students aged 18-29 years old (88 males) studying in Singapore completed twelve questionnaires that measured autistic traits, anxiety and depressive symptoms and the five examined mediators. Multiple mediation analyses were conducted using the bootstrapping method.

**Results:** A significant positive relationship was found between autistic traits and anxiety. Most of the examined mediators were significant for the total anxiety and depressive symptoms mediation models. Aversive sensory experiences were the strongest mediator across all anxiety and depressive symptom mediation models. Some mediators were specific to particular types of anxiety:only prevention from/punishment for preferred repetitive behaviors and frequent aversive sensory experiences mediated the relationship between autistic traits and generalized anxiety or obsessive-compulsive symptoms. Social competence had the largest mediation effect in social anxiety, but was not a significant mediator of total anxiety symptoms, generalized anxiety or OCD symptoms. Teasing experiences mediated the relationship between autistic traits and total or social anxiety as well as depression, but not generalized anxiety or OCD symptoms.

**Conclusions:** Our findings are consistent with Rosbrook and Whittingham (2010) and provide some evidence for Wood and Gadow's (2010) conceptualization of anxiety in ASD, although clearly these findings also need to be replicated with clinical samples. Supporting individuals with high autistic traits in managing aversive sensory experiences may lead to decreases in many anxiety symptoms. Our results also suggest that interventions for anxious and depressive symptomatology in individuals with high autistic traits may be more effective if they target relevant autism-related stressors alongside core anxiety symptoms (i.e. social competence and decreasing or preventing teasing in socially anxious individuals with high autistic traits; managing repetitive behaviors in those with high autistic traits and generalized anxiety or obsessive compulsive symptoms). Possible implications for understanding and managing anxiety in clinically diagnosed individuals with ASD as well as in those with diagnosed anxiety disorders without ASD are discussed.

**174.064 64** Artificial Neural Networks Show Complex Interplay Among Risk Factors Related to Pregnancy, and Peri and Post Natal Period That May Contribute to Autism: A Pilot Study. E. Grossi*[1], F. Veggo[1], F. Muratori[2] and A. Narzisi[3], (1)*Villa Santa Maria Institute*, (2)*Stella Maris Scientific Institute*, (3)*University of Pisa - Stella Maris Scientific Institute*

**Background:** Autism Spectrum Disorder (ASD) is a multi-factorial disease, where a single risk factor unlikely can provide comprehensive information. Moreover, due to the non-linearity of biomarkers, traditional statistic is often unsuitable and underpowered to dissect their relationship. Recent epidemiological studies have pointed out a number of pregnancy and peri-post natal factors which, contributing to focal brain inflammation, predispose to ASD development.

**Objectives**: The aim of the study is to assess the prevalence and natural relationships among 23 potential risk factors in pregnancy history and peri and post natal events in a group of 45 autistic children in comparison with 54 typical children.

**Methods**: Traditional statistics (Principal Component Analysis-PCA) and Artificial Neural Networks (Auto-CM system) were applied to highlight the associations among variables under study. Auto-CM is a special kind of Artificial Neural Network developed at Semeion Research Institute( Rome) and successfully applied in many

complex chronic degenerative diseases, able to find out consistent trends and associations among variables creating a semantic connectivity map. The matrix of connections, visualized through minimum spanning tree filter, takes into account nonlinear associations among variables and captures connection schemes among clusters.

**Results:** An higher prevalence of potential risk factors was observed in 18 out of 23 risk factors in autistic group; for five of them the difference in prevalence was statistically significant ($p<0.05$) despite the relative small sample size: exposure to solvent or paints during pregnancy (25% autism vs. 3.8% Typicals), pregnancy complications( 50% autism vs 32% Typicals), perinatal complications ( 36.4 % autism vs 20.75% Typicals), stressful life events (mean number per woman: 0.49 autism vs. 0.06 Typicals), early antibiotic therapy after birth(25.04% autism vs 13.21% Typicals). Auto-CM system, at variance with PCA, was able to point out complex relationships among variable under study showing a convergence of branches of risk factors toward autistic outcome.

**Conclusions:** The general prevalence of potential risk factors in pregnancy history and peri and post natal events is higher in autistic group in comparison with Typicals. According to univariate analysis exposure to solvent or paints during pregnancy, pregnancy complications, perinatal complications stressful life events and early antibiotic treatment appear as key players. Artificial neural networks help to highlight the underlying interaction scheme among different factors on study showing a complex matrix of connections among them.

**174.065 65** Behavior Profiles of Children with Attention Deficit Hyperactivity Disorder Behaviors and Children with Autism Spectrum Disorder on the Parent PDD Behavior Inventory. I. L. Cohen*, *New York State Institute for Basic Research in Developmental Disabilities*

Background: Substantial overlap exists between Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD). Etiologically, similarity exists in genetic liability for the two disorders. Phenotypically, comorbidity exists between ASD and symptoms of ADHD with rates varying between 28% and 92% and both groups have similar problems with social cognition. Where there is comorbidity between ASD and ADHD, studies suggest that a more severe phenotype exists: increased oppositional and anxiety behaviors, decreased IQ, and adaptive skills and worse response to intervention.

In gathering information on the PDDBI prior to clinical observation, we came across highly unusual profiles indicating very severe behavior problems along with relatively intact communication skills leading us to expect to see a high-functioning child with ASD. To our surprise, both clinical observations and assessment with the ADOS-G indicated the child did not have ASD. Instead diagnoses of ADHD, and/or anxiety/mood disorders were provided.

Objectives: The purpose of this study was to investigate this phenomenon by examining similarities and differences in parent PDDBI ratings of children with ASD and children with ADHD behaviors.

Methods: The sample consisted of 139 children (2.4 to 13.8 years) referred for differential diagnosis. Parent ratings of children with ASD (with and without ADHD behaviors) were compared with parent ratings of children with ADHD behaviors who did not have ASD (the ADHD group) using the PDD Behavior Inventory (PDDBI), a rating instrument that is age-standardized on children with ASD and which assess both maladaptive behaviors and adaptive skills. Analyses included MANOVAs and classification trees (CART analysis).

Results: The ADHD group's maladaptive behaviors were rated as **more** severe than the ASD group, especially on those domains assessing fears and aggression. Further, the ADHD group was rated as having greater severity of fears and aggression when compared with those in the ASD group who also had comorbid ADHD behaviors and better expressive language ability than the ASD group (especially when compared with those in the ASD group with comorbid ADHD behaviors). Using four domains from the PDDBI (FEARS, EXPRESS, AROUSE and RITUAL), CART classified 94% of the ASD group and 87% of the ADHD group correctly.

Conclusions: These data extend findings from previous studies and suggest that a unique ADHD profile may exist for children with ADHD on the

PDDBI. It is hypothesized that the increased severity of fears and aggression in the ADHD group reflects their increased ability to communicate these problems to others. Children with both ASD and ADHD behaviors were more severely affected than their ASD cohorts whose parents did not report ADHD behaviors. As a group, they were the ones whose social communication scores and scores for classic ASD problems were similar to the standardization sample while those ASD children who did not have ADHD traits presented with a more mild phenotype. It is predicted that some of these children will likely have a different genetic background than the ASD-ADHD group based on our research showing that an X-linked genotype linked to serotonin metabolism affects the severity of parent PDDBI scores for males with autism.

**174.066 66** Co-Occurring Social Anxiety Disorder in Adults with Autism Spectrum Disorder. B. B. Maddox* and S. W. White, *Virginia Polytechnic Institute and State University*

Background: Social Anxiety Disorder (SAD) tends to present in adolescence and persist into adulthood (Alfano et al., 2006), and symptoms of social anxiety are fairly common among people with ASD (e.g., Chang et al., 2012). Few studies have examined the presence of SAD in adults with ASD, but recent estimates in the range of 30% suggest that SAD is also common in this population, when intellectual disability is not present (Kreiser & White, 2013). A better understanding of co-occurring social anxiety, including its prevalence and how to accurately assess it, is critical for adults with ASD.

Objectives: The primary objective was to examine the prevalence and manifestation of SAD in a non-treatment seeking sample of adults with ASD. Most research on social anxiety in individuals with ASD has focused on the physiological symptoms and behavioral avoidance, largely ignoring the influence of socially anxious cognitions. The current study aimed to collectively assess all three dimensions (i.e., physical, behavioral, and cognitive) of social anxiety, in order to fully explore the experience of social anxiety phenomenologically in ASD.

Methods: The sample currently consists of 25 individuals with ASD (16-45 years old; 14 males) who participated in a one-session eye-tracking study. The target sample size of 30 participants is expected by December 2013. All participants have a confirmed ASD diagnosis, based on the ADOS, Second Edition (ADOS-2; Lord et al., 2012) and clinical interview. They also completed a brief cognitive assessment and the social anxiety module of the Anxiety Disorders Interview Schedule (ADIS; Brown et al., 1994). The ADIS was conducted by clinicians trained to reliability and knowledgeable about the distinctions between ASD characteristics and SAD symptoms.

Results: Of the 25 participants, 12 (48%) met diagnostic criteria for SAD on the ADIS. Their qualitative descriptions highlight the bi-directional relationship between social anxiety and the social deficits associated with ASD. For example, one participant explained: "I don't know what to do at a party. I have no idea how to keep a conversation going. I might ramble, and then people will judge me and think I'm odd or stupid." Several participants also emphasized the role of past peer victimization in the development of their social anxiety symptoms, and the contribtion of social anxiety to isolation and loneliness. Of the 13 participants without SAD, many expressed a dislike of or disinterest in social situations, but they exhibited no explicit fear of negative evaluation from others.

Conclusions: These findings demonstrate that many adults with ASD are acutely aware of their social difficulties and experience impairing social anxiety as they face increasing social complexities during adulthood. The accurate assessment and differential or dual diagnoses of ASD and SAD are challenging, and more research in this area is greatly needed, particularly with adults. Examining the presence or absence of the cognitive symptoms of SAD (e.g., concerns related to self-embarrassment and negative evaluation by others) may be useful for phenotyping and treatment planning with individuals with ASD. These cognitions may be related to social insight and social motivation.

**174.067 67** Development of the Autistic Catatonia Questionaire. D. Hare* and J. Breen, *University of Manchester*

Background:

A catatonic presentation manifesting in early to mid-adolescence is reported in about 8% of people with autism spectrum disorders, with core features of being very still for long periods of time, getting 'stuck' when trying to do something, difficultly stopping actions once they have been

started, difficulties in initiating actions, moving very slowly and taking a long time to finish actions and requiring physical and /or verbal prompts in order to complete actions. To date, little is known about the aetiology, phenomenology and course of such 'autistic catatonia', a state of affairs that isexacerbated by the current lack of appropriate clinical and research assessment tools.

Objectives:

In order to facilitate objective clinical and research work into the nature and treatment of "autistic catatonia", the initial aim of the current study was to develop a psychometrically sound third-party observational assessment of catatonic symptoms as presenting in people with ASD.

Methods:

The 34-item *Autistic Catatonia Questionnaire* (ACQ) was developed from extant reports of autistic catatonia and measures of catatonic symptomatology and comprises six core features of autistic catatonia and an additional 28 items covering other aspects of repetitive, motoric and sensory functioning. Items are scored for presence, frequency and severity. Preliminary ACQ data, together with data from the Repetitive Behaviour Scale and the Glasgow Depression Scales and relevant demographic and contextual information, was obtained from relatives and supporters of adolescents and young adults with ASD living in the United Kingdom

Results:

Date from the relatives and supporters of 99 participants with a diagnosis of ASD aged between 12-25 years ACQ data were initially coded to obtain *core autistic catatonia score, core severity score* and *core frequency scores.* Preliminary data analysis indicated the six core symptoms were relatively common in the sample, with a mean of 2.38 symptoms being reported and 85% of participants displaying least one core symptoms either currently or in the past. Mean core autistic catatonia score was 7.48, with those with existing catatonia diagnoses having significantly higher numbers of core symptoms and core frequency scores. GDS-LD scores were correlated with the number of core symptoms and the core autistic catatonia score

Conclusions:

The preliminary data suggest that the ACQ shows promise as a valid and easy to use tool for the clinical and research assessment of autistic catatonia. Further work is on-going to examine the reliability of the measure and to investigate the relationship of catatonic symptomatology as measured by the ACQ with actigraphically assessed activity levels and circadian functioning.

**174.068 68** Endocrine Profile at Puberty in Autism Spectrum Conditions. L. Ruta*[1], A. Pohl[2], L. Reale[3], A. Nicolosi[4], L. Mazzone[5], D. Mazzone[6], M. Caruso[4], K. Taylor[7] and S. Baron-Cohen[8], (1)*Division of Child Neurology and Psychiatry, Department of Developmental Neuroscience, Stella Maris Scientific Institute*, (2)*Autism Research Centre, University of Cambridge*, (3)*Division of Child Neurology and Psychiatry, Department of Paediatrics, University of Catania*, (4)*Division of Pediatric Endocrinology, Department of Paediatrics, University of Catania*, (5)*Child Neuropsychiatry Unit, Department of Neuroscience, I.R.C.C.S. Children's Hospital Bambino Gesù*, (6)*University of Catania*, (7)*Department of Clinical Biochemistry, Addenbrookes Hospital*, (8)*University of Cambridge*

Background:

Autism spectrum conditions (ASC) are characterized by a striking male prevalence. Converging evidence suggests that sex hormones may play a role in the link between ASC and maleness. Puberty is a crucial phase of sexual development where the sexual differentiation of the brain, primarily established prenatally, is actively maintained. Puberty and sex hormone profile at puberty have not been yet systematically studied in ASC.

Objectives:

(i) To evaluate the physical and pubertal development in children with ASC, and (ii) To investigate the sex hormone profile of children with ASC during puberty.

Methods:

The study was conducted at the University Hospital 'G. Rodolico' in Catania, Italy and approved by the Local Research Ethics Committee. We studied n = 81 male children, n = 43 having a clinical diagnosis of ASC and n = 38 male age- and IQ-matched typically developing children. A physical and growth examination was conducted using the following measures: head circumference

(HC), height (H) weight (W), body mass index (BMI), estimation of the target height (TH), Z-scores (standard deviation scores) for HC, H, TH and BMI, Tanner stages (Tanner, 1969) for pubic hair and genitalia. Development of axillary hair, distribution of body hair and presence of acne were determined by visual inspection. Testicular volume was assessed using an orchidometer. The following hormones were analyzed in the serum: androstenedione, dehydroepiandrosterone sulfate (DHEA-S), total-testosterone, sex-hormone binding globulin (SHBG), free-testosterone, progesterone, estradiol, cortisol, *luteinizing hormone (*LH) *follicle-stimulating hormone* (FSH), growth hormone (GH), IGF-1.

Results:

Educational level, socioeconomic status, diet preferences, and exercise were investigated and no between-group differences were reported (chi-square tests, all $p>0.5$). No group differences in H, W, BMI and TH were found. Children with ASC at Tanner stage 2 ($n=22$, age=9.7 ± 1.16 years) were approximately 8 months younger than controls ($n=26$, age=10.3 ± 0.7 years) and this difference was significant ($p=0.038$). The sex-hormone profile showed significantly higher levels of estradiol, progesterone and LH in ASC males. SHBG was significantly lower in ASC compared to controls, leading to significantly higher levels of free-testosterone. Mean levels of androstenedione, total-testosterone, GH and IGF-1 were all increased in the ASC group but between-group differences did not reach significance.

Conclusions:

Male children with ASC started puberty (Tanner stage 2) approximately 8 months earlier than controls and displayed an activation of the sex steroid pathway as demonstrated by higher levels of free-testosterone, estradiol, progesterone and LH. These preliminary results suggest that male children with ASC may have a different hormone profile, and a different start and trajectory of puberty, compared to typically developing children.

**174.069 69** Family Driven Goals Improve Sleep in Children and Youth with Autism Spectrum Disorder. K. Sohl*[1], J. Taylor[2], D. L. Coury[3], N. Madduri[4], P. Green[5], A. M. Neumeyer[6], T. Katz[7], S. E. Levy[8] and B. A. Malow[9], (1)*University of Missouri*, (2)*National Initiative for Children's Health Care Quality*, (3)*Nationwide Children's Hospital*, (4)*Vanderbilt University School of Medicine*, (5)*Holland Bloorview Kids Rehabilitation Hospital*, (6)*Massachusetts General Hospital*, (7)*University of Colorado*, (8)*Children's Hospital of Philadelphia*, (9)*Vanderbilt University Medical Center*

Background:

Sleep concerns are common in children with autism spectrum disorder (ASD) and are estimated to affect 50-80% of children with ASD. Children with ASD commonly experience sleep onset delay, night time awakenings and bedtime resistance. Despite this high incidence, studies show that providers identify sleep concerns in only 8% of patients.

The Autism Intervention Research Network on Physical Health (AIR-P)/ Autism Speaks Autism Treatment Network (AS ATN), in coordination with NICHQ (National Initiative for Children's Healthcare Quality), established a Learning Collaborative to Improve Care for Children with Autism Spectrum Disorder (ASD). Seven teams in this learning collaborative supported families to track sleep and improve sleep using quality improvement methodology.

Objectives:

The primary aim was to identify a way to improve sleep in children with ASD by collaborating with families. The secondary aim was to identify a systematic process for clinicians to ask, assess, and address sleep concerns and then adjust based on family goals and family reported data.

Methods:

Seven AIR-P/AS ATN sites were chosen to participate in the insomnia stream. An "N of 1" approach was used by each site to intensively work with one child and his or her family to optimize care for insomnia. Children were screened to identify those with insomnia. Then, we met with families to assess their willingness to test changes with their child, and report on their progress weekly. If so, family-directed goals and feasible strategies were set for the family to try. Families reported data on their goals with up to four metrics. The improvement team coached families weekly based on their feedback about their child's progress. The seven improvement teams also met biweekly via webinar to discuss, share learning and review data. The learning collaborative tested small tests of change with

each family and as a group, including families of varying needs and complexity levels. Sites developed systems to ask about sleep at each visit and set family goals for addressing sleep concerns.

Teams gathered data from families on a daily and/or weekly basis regarding sleep, using innovative tools including Research Data Electronic Capture (REDCap), Google Drive, FluidSurvey, text messaging, phone calls and electronic medical record portals.

Results:

42 families participated in the Insomnia Stream. Through continuous process improvement, teams developed a system that allowed families to set family-led goals and achieve success. Median time to one sleep-related improvement was 5 weeks. Median time to two sleep-related improvements was 7.5 weeks. Examples of sleep-related improvements include reductions in time to fall asleep, less resistance at bedtime, and decreased night wakings.

Conclusions:

Sleep concerns are common for children with ASD. Sleep is underidentified by providers caring for these children. By developing a process that systematically assesses sleep concerns and sets family-driven goals for improvement with consistent follow-up, sleep concerns may be reduced. Through this process teams from across North America engaged in small tests of change to develop a system that can be spread to other providers and settings.

**174.070 70** Food Selectivity and Sensory Sensitivity Subtypes in Children with ASD: A Cluster Analysis. L. Fava*, M. Esposito and K. Strauss, *Autism Treatment and Research Center "Una Breccia nel Muro"; Rome, Italy*

Background:

Studies examining food selectivity (FS) conclude that children with ASD demonstrate high levels of reluctance to try new food, restricted repertoire of foods and fewer foods intakes within food categories. Factors that parents felt influence selectivity were: texture, appearance, taste, smell, temperature, or food presentation. In addition, it is also possible that the mealtime behavior problems frequently seen in children with ASDs may reflect problems with sensory sensitivity. Thus, it is suggested that food selectivity is not a unique characteristic of autism, but reflect sensory defensiveness. Recent studies primarily relied on categories of over- and under-responsiveness representing distinct categories of sensory processing (SP). Nevertheless, tactile defensiveness and oral defensiveness may be part of a larger problem in modulating sensory input which can take different forms. A behavior topography of mouth stuffing might result from over-responsiveness difficulty with textures, under-responsiveness difficulty of perceiving sensations, and/or seeking behavior for the purposes of oral stimulation. This suggests that sensory under- and over-responsivity may co-exist in children with autism as found by Ben-Sasson et al. (2007) proposing a mixed pattern of SP in ASD indicative of a common etiology underpinning poor sensory modulation.

Objectives:

The aims of the present study were: (a) to examine the patterns of SP and FS difficulties within autism and (b) to examine the relationship between SP and FS patterns with related dietary issues.

Methods:

Fifty children with autism spectrum disorder participated in this study. Diagnostic status was determined based on the DSM-IV, ADI-R, ADOS-G and independently confirmed. Participants were aged 25 to 72 months (mean=50.42, SD=19.22) with 42 (84%) being male. All participants were registered with the Early Intervention Program at the Autism Treatment and Research Centre Una Breccia nel Muro. SP was assessed via the Sort Sensory Profile (SSP, McIntosh et al., 1999), FS via the Brief Assessment of Mealtime Behaviors In Children (Hendy et al., 2012), dietary intake and gastrointestinal problems via a survey adapted from Badalyan & Schwartz (2012) as well as the BMI.

Results:

Preliminary results confirmed that the majority (~80%) of participants exhibited SP dysfunction, particularly in Auditory Filtering, Underresponsive/Seeks Sensation, Taste/Smell Sensitivity domains. Notably, most participants (~62%) demonstrated differences from typical

BMI percentiles, restricted dietary intakes (~56%), gastrointestinal problems (~64%) and mealtime behaviors perceived as problematic by parents (~68%). Detailed analysis that is subject to presentation at the congress is addressed via cluster analysis including sensory processing and mealtime behaviors. It is expected that at least 3 distinct SP/SF subtype pattern can be confirmed where food refusal, limited variety, under-and over-responsiveness are not separately represented but topographically coexists. Differences are expected to be better represented by its contextual function, supporting broader subtypes of modulation difficulties. In deep analysis is completed applying regression analysis in order to examine the association of SP/FS patterns with dietary intake, gastrointestinal problems and BMI.

Conclusions:

This study extends previously published work by: evaluating patterns of SP and FS difficulties, mealtime behaviors, gastrointestinal problems and nutritional intake by applying state-of-the-art cluster analysis techniques.

**174.071 71** In-Depth Understanding of Anxiety Experienced By Children and Adolescents with ASD, and Impact on the Family. J. Palilla*[1], M. South[1] and J. Rodgers[2], (1)*Brigham Young University*, (2)*Newcastle University*

Background: Among adolescents and school-aged children with ASD, anxiety-related concerns are among the most common presenting problems (White et al., 2009). Research has shown that anxiety may increase their poor social skills and have a substantial negative impact on a person's ability to engage in activities in the home, at school or in general community activities (White, Schry & Maddox, 2012). Both increased rates of aggression and high social understanding are also associated with increased anxiety. However, the underlying nature of anxiety symptoms in ASD is still unclear. A key obstacle for this area of research is that current measures of anxiety may not always be appropriate for assessing individuals with ASD.

Objectives: This exploratory study was designed to better characterize the co-occurring symptoms of anxiety in individuals with autism as described by their mothers. The rich descriptions gathered from a parent interview were used to determine how well the reported features of anxiety on a standard pencil-and-paper questionnaire are representative of anxiety or characteristics of ASD.

Methods: Mothers of children ages 12-16 diagnosed with ASD completed the Spence Children's Anxiety Scale-Parent Survey Version (SCAS, Spence, 1998) and the Social Responsiveness Scale (SRS; Constantino, 2004). Following the completion of the surveys, each mother was interviewed using the Spence Children's Anxiety Scale–Parent Interview developed by Dr. Jacqui Rodgers and Ruth Jamieson of Newcastle University. Mothers answered questions about 1) statements on the SCAS-P most relevant to their child; and 2) any other anxiety-producing situations not captured by the SCAS. Interview questions specifically addressed the child's anxious thoughts, emotions, physical symptoms, as well as the context in which the anxious response was developed. Mothers were asked to describe the impact their child's anxiety has on the family.

Results: 35 mothers (20 with ASD children; 15 with non-autism anxious children) completed the study. Mothers of ASD children endorsed more statements on the Obsessive-Compulsive Disorder, Separation Anxiety and Social Anxiety subscales of the SCAS. Statements such as "My child can't seem to get bad or silly thoughts out of his head" and "My child feels afraid that he will make a fool of himself in front of people" were endorsed by a significant portion of ASD mothers. Mothers of ASD children tended to attribute the development of the anxiety to school situations and often reported that they felt their child's thoughts and worries were reasonable given the situation their children faced at school. All mothers described significant levels of family interference due to anxiety.

Conclusions: Initial qualitative analysis of the data reveals that the anxious features reported by mothers of children with ASD are significant and impact both the child and the family. This suggests that assessing for anxiety in children on the spectrum should be an integral part of treatment. Furthermore, many of the socially anxious symptoms were attributed to either the start of school or experiences at school. This suggests that early intervention for school preparation may be beneficial for children with ASD.

**174.072 72** Investigation of Individual Factors Associated with Anxiety in Youth with Autism Spectrum Disorder. A. Dubin*, R. G. Lieberman-Betz and M. Lease, *University of Georgia*

Background: Prior research has indicated anxiety symptoms and disorders are highly prevalent in youth with autism spectrum disorder (ASD) and may impart additional impairment (Van Steensel, Bogels, & Perrin, 2011). The extant literature yields conflicting findings regarding factors related to anxiety (e.g., cognitive functioning, social impairment) and the nature of such relations. Validating and extending prior anxiety risk factor research is necessary to improve assessment and guide treatment.

Objectives: To identify individual factors associated with anxiety risk and explore whether cognitive functioning moderates such associations in a large sample of youth with ASD.

Methods: The present study used extant data from the Simons Simplex Collection (SSC), a database of genotypic and phenotypic information obtained from 4- to 18-year-old youth with ASD (n=2662).

A dichotomous anxiety risk outcome variable was produced from scores on parent-rated *Child Behavior Checklist* (CBCL; Achenbach & Rescorla, 2001) DSM-IV Anxiety Problems scale based on the CBCL-defined cut point (scores 65 and above = high risk). Factors with hypothesized relations to anxiety included social withdrawal, adaptive social behavior, autism severity, intellectual functioning, age, and gender. Factors were derived from the *Aberrant Behavior Checklist* (ABC; Aman et al., 1985), *Autism Diagnostic Observation Schedule* (ADOS; Lord et al., 2002), *Vineland Adaptive Behavior Scales, 2nd Edition* (Vineland-II; Sparrow et al., 2005), and multiple measures of intellectual functioning (e.g., *Differential Ability Scales, 2nd Edition* [DAS-II; Elliot, 2007]).

A multivariate logistic regression model was built to examine the factors independently associated with anxiety risk while controlling for all other factors. Then, a hierarchical logistic regression model was created to investigate whether intellectual functioning moderated the relation between hypothesized factors and anxiety risk. Finally, the nature of any significant moderation was probed by examining the conditional effects of factors on anxiety risk for youth with high and low cognitive functioning.

Results: Results from the first model indicated anxiety risk was related to four individual factors at the $\alpha$=.05 level. High-risk youth were less likely to be female (odds ratio [OR] = 0.69, 95% CI [0.54, 0.89]) and more likely to have average or greater cognitive functioning (OR = 1.96, 95% CI [1.58, 2.43]). Likelihood of being classified as high risk increased as age (odds ratio = 1.11, 95% CI [1.08, 1.13]) and social withdrawal increased (OR = 1.07, 95% CI [1.06, 1.09]).

Moderation analysis indicated intellectual functioning moderated the relation between adaptive social behaviors and anxiety risk (OR = 0.97, 95% CI [0.96, 0.99], $p < .05$). Simple slope analyses revealed that higher adaptive social behaviors were associated with membership in the high anxiety risk group for youth with lower cognitive functioning (OR = 1.02, CI [1.00, 1.03]). There was no relation between adaptive social behaviors and anxiety risk for youth with average or higher cognitive functioning.

Conclusions: Results from the present study provide support for previously identified risk factors; however, further investigation is necessary to uncover additional risk factors and to explore how their relation to anxiety differs across individuals with ASD and varying levels of cognitive functioning.

**174.073 73** Antibrain Antibodies in Children with Autism Spectrum Disorder and in Mothers Are Associated with More Severe Cognitive and Behavioural Profiles. I. S. Piras*[1], L. Haapanen[2], V. Napolioni[1], R. Sacco[1], J. Van de Water[2] and A. M. Persico[3], (1)*University Campus Bio-Medico*, (2)*UC Davis*, (3)*Mafalda Luce Center for Pervasive Developmental Disorders*

Background: Previous work reported the detection of antibrain autoantibodies in the peripheral blood of children affected with ASD, specifically reacting with the cerebellum. Presence of these autoantibodies has been associated with lower adaptive and cognitive function, as well as with core symptoms of autism. Additionally, subsets of mothers of affected children produce IgG directed against fetal proteins, which during pregnancy most likely pass into the fetal circulation and reach the brain, since prenatally the blood-brain barrier is still permeable. These maternal antibodies have been associated with

autism, lower expressive language scores and increased irritability using the Aberrant Behavioral Checklist.

Objectives: To assess: (1) the prevalence of 45 and 62 kDa autoantibodies among autistic children and unaffected siblings, (2) the prevalence of 37, 39, and 73 kDa antibrain antibodies in mothers of affected children, and (3) the clinical, cognitive and behavioural correlates of positive maternal or patient autoantibody status.

Methods: Antibrain autoantibodies were measured in plasma samples collected from 355 Italian autistic patients, 142 unaffected siblings and 333 mothers using Western Blot technology. Data were analyzed using the chi-squared test or the non-parametric Mann-Whitney U test. Nominal $P<0.05$ was considered significant.

Results: Antibrain autoantibodies were detected in 48/355 (13.5%) ASD and 26/142 (18.3%) unaffected siblings ($P=0.200$, n.s.). Among autistic children, the 45 kDa autoantibody is significantly associated with cognitive impairment and lower scores in all four Vineland Adaptive Behavior Scales (both $P<0.05$). The 62 kDa autoantibody is specifically associated with motor stereotipies and greater birth order ($P<0.05$). Maternal antibrain antibodies (37, 39 and 73 kDa) were detected in 137/355 (41.1%) mothers of ASD children. The presence of maternal antibodies, either alone or in combination, is correlated with impaired verbal and non-verbal language development, with sleep/wake cycle disturbances in their autistic children ($P<0.05$), and with neurodevelopment delay ($P<0.01$), as defined by principal component 3 in Sacco et al., Autism Res 3:237-252, 2010. Finally, we observed that antibrain autoantibody production is familial: presence of the 62 kDa Ab in the child is significantly associated with presence of the 39 and/or 73 kDa antibodies in their mother. Furthermore, these two maternal antibodies are in turn associated with more frequent autoimmune disease among first-degree relatives ($P<0.05$ and 0.01, respectively).

Conclusions: Our results confirm and extend previous observations in an ethnically distinct sample, providing further evidence of a strong pathomorphic contribution of antibrain antibodies to autism. The prevalence of antibrain autoantibodies does not differ between autistic and unaffected siblings, indicating that within the same sibship they do not confer increased risk of developing autism. However, they negatively influence autism severity, resulting in cognitive impairment and lower VABS scores in patients positive for antibrain antibodies; lower verbal and non-verbal language development, as well as wake/cycle disturbances in autistic children exposed to maternal antibrain antibodies. Antibrain antibodies are part of a broader familial liability to autoimmunity. Genetic factors conferring this vulnerability are currently under investigation.

**174.074 74** Effects of Parental Stress and General Well Being, and Parent Child Interaction. A. San José Cáceres*[1], V. Slonims[2], P. Howlin[3], E. Pellicano[4] and T. Charman[5], (1)*King's College*, (2)*Guy's and St Thomas' NHS Foundation Trust*, (3)*King's College London, Institute of Psychiatry*, (4)*Centre for Research in Autism & Education, Institute of Education*, (5)*King's College London*

**Background:**

Dyadic synchronous communication between parent and child is known to be related to optimal pathways of social and cognitive development from a young age. For instance, synchrony has been shown to act as a predictor of later language (Siller & Sigman, 2008; Aldred et al., 2008) and symbolic play development (Feldman & Greenbaum, 1998). Asynchrony has been, on the contrary, associated to a decreased number of language learning opportunities (Reddy et al., 1997). In the case of children with ASD, where social development follows atypical pathways, parental synchrony plays a major role in the socio-communicative development of the child, and possible asynchrony can affect children's development. Parents of children with ASD have been reported to have high levels of stress indicated by elevated cortisol levels and this is greater than those with children with other developmental disabilities (Dykens & Lambert, 2013). Levels of stress are related to levels of dependency functional impairment and cognitive levels in children with ASD (Koegel et al., 1992) and may compromise the parent-child relationship (Feldman & Eidelman, 2004). It is possible that such factors affect early intervention in autism (Osborne, et al., 2008).

**Objectives:**

To explore levels of stress and well-being in parents whose children have been diagnosed with ASD within the last 12 months, and to see how this may be related to severity of autism symptoms. Also, to study how parental stress levels may modulate synchronous communication with their child. Lastly, to explore the indirect effects of the NAS EarlyBird group-based parenting programme (Shields, 2001) – widely used in the UK – in parental stress levels and its relation to parent-child interactions.

**Methods:**

Eighteen families from different boroughs in London who attended the EarlyBird programme were assessed two weeks before and after the programme (3-months interval). Parents filled in questionnaires regarding their view of their parenting competence (PSOC), well-being (WEMBWS) and their level of stress (PSI and APQ Stress sub-scale). Children were assessed prior to the programme using ADOS, SRS, SCQ and Mullen Scales of Early Development. At both assessment points, families were interviewed regarding their child's adaptive skills using the Vineland Adaptive Behaviour Scales and were video-recorded playing with their child for 10mins to assess parent-child interaction following the DCMA schedule (Aldred, Green, & Adams, 2004).

**Results:**

At baseline, parental stress (measured with PSI) and self-confidence correlated significantly with autism symptoms from the SRS ($r$ = .55, $p$ = .03; $r$ = .54, $p$ = .04 respectively) but not with the intellectual ability of the child. All baseline measures of parental mental health were analysed in relation to the number of synchronous communicative acts during a play interaction, but no significant results were found. Post-treatment data are currently being collected.

**Conclusions:**

While parental stress levels seem to be highly associated with the severity of ASD, it is not with the way parents communicate with their children. It remains to be explored whether the attendance to the EarlyBird programme increases parental well-being and if this relationship is affected by the severity of ASD.

**174.075 75** Comparison of Rsa during a Relaxation Task Between ASD, Anxiety, & Controls. L. Guy*[1], M. C. Souders[2], C. M. DeLussey[3], C. M. Kerns[4] and J. Herrington[5], (1)*The Children's Hospital of Philadelphia*, (2)*University of Pennsylvania School of Nursing/The Children's Hospital of Philadelphia*, (3)*Center for Autism Research, The Children's Hospital of Philadelphia*, (4)*Drexel University*, (5)*University of Pennsylvania*

Background:

Respiratory sinus arrhythmia (RSA), a measure of heart rate variability, reflects the action of the parasympathetic nervous system on heart rate. A higher RSA is associated with better physical and emotional health, and a more adaptive response to changing environmental demands. Recent studies have used RSA to better understand the anxiety symptoms and social deficits in ASD. Social impairment is a defining feature of ASD, and anxiety is a commonly occurring comorbid condition with rates at approximately 40%. To our knowledge no studies have yet compared RSA for individuals with ASD with and without anxiety to individuals with an anxiety disorder alone.

Objectives:

The aim of this study was to compare RSA during a relaxing task across four groups of participants who were well-characterized using gold standard measures for ASD (i.e., the ADOS) and Anxiety (i.e., the ADIS). It was hypothesized that individuals with ASD regardless of their anxiety status would have a lower RSA than either the Anxiety alone group or controls because of social impairments associated with the disorder. It was also predicted that RSA would be related to better socialization skills and executive function skills involved in behavior regulation.

Methods:

Participants included a total of 68 children between the ages of 7-17 who were grouped according to the presence or absence of (1) ASD and (2) an Anxiety disorder, yielding four groups: ASD only, ASD plus anxiety disorder, anxiety disorder without ASD, and typically developing controls (TDC). IQ was assessed using the DAS-II; executive function skills were assessed by BRIEF parent report; behavioral function was assessed by CBCL; and socialization skills were assessed by the Vineland (VABS) parent interview. ECG data were collected using the Biopac MP150 system and a standard Lead-II

configuration, at a sampling rate of 1000 Hz. The relaxation task involved participants watching a 5-minute video of a dynamic beach scene with gentle rolling waves.

Results:

ANOVAs indicated no significant group differences for age, F(4,67)=.249, p=ns (ASD only M=12.59; ASD plus anxiety M=11.08; Anxiety M=11.50, TDC M=12.25) or composite IQ, F(4,67)= .902, p=ns, (ASD only M=105; ASD plus anxiety M=97; Anxiety M=104; TDC M=110). There was a significant group main effect for RSA during the relaxation task, F(4,67)= 2.62, p=.042. Follow-up analyses showed this was driven by the ASD only group being significantly lower than the TDC group, p=.034. There were no significant differences between the other groups. RSA was positively correlated with adaptive Socialization skills, r=.198, p=.054 and negatively correlated with social problems on the CBCL, r=-.220, p=.036. There was a significant negative correlation between RSA and BRIEF Behavior Regulation skills, r=-.205, p=.046.

Conclusions:

Study findings supported the hypothesis that individuals with ASD would have significantly lower RSA than controls, and that RSA is associated with social functioning and behavior regulation. Counter to predictions, RSA was not associated with anxiety symptoms in the present sample. Data analysis is ongoing.

**174.076 76** Empathy, and Autistic Traits in Children with Attention-Deficit/Hyperactivity Disorder. L. Ruta*[1], R. Siracusano[2], E. Germanò[3] and A. Gagliano[4], (1)*Stella Maris Scientific Institute*, (2)*National Research Council of Italy (CNR)*, (3)*Università di Messina*, (4)*University of Messina*

Background: Children with attention-deficit/hyperactivity disorder (ADHD) often display significantly more comorbid autistic traits (ATs) compared with their peers without ADHD. Furthermore, previous research demonstrated that the group with both ADHD and ATs show significantly more neuropsychological and interpersonal deficits, as well as more emotional dysregulation.

Objectives: to investigate empathy and autistic traits in children with ADHD as compared with children with Autism Spectrum Conditions (ASD) and typically developing children (TYP).

Methods: n=32 ADHD children (combined type), n=35 ASD children and n=77 TYP children were evaluated using the Italian version of the Child Autism Spectrum Quotient (C-AQ) and the Child Empathy Quotient (C-EQ). All the children were assessed at the Policlinic University Hospital "AOU G. Martino" in Messina, Italy, they were all males and matched for age and IQ. ADHD and ASD diagnoses were made according to the DSM-IV criteria and supported by the Conners 3rd Edition scale – parent version and the Autism Diagnostic Observation Schedule (ADOS), respectively.

Results: at the C-AQ, the ADHD and ASD group both showed significantly higher scores compared to the TYP group, with the ASD group showing significantly higher scores compared with the ADHD group. At the C-EQ the ADHD and ASD groups showed comparable scores with each other and significantly lower scores compared to TYP children.

Conclusions: our results show that ADHD children display significantly higher autistic traits and lower empathy compared to typically developing children.

**174.077 77** Do ASD Symptoms at 2 Years Influence the Prediction of Childhood Sleep Problems and Anxiety from 2- to 8-Years?. J. Davis*[1], A. L. Richdale[1] and S. M. Cotton[2], (1)*La Trobe University*, (2)*University of Melbourne*

Background: Research has demonstrated a link between sleep difficulties and anxiety amongst typically developing children and children with ASD. Both anxiety and poor sleep are common in children with ASD and they are 2-3 times more likely to experience sleep and anxiety problems than are typically developing children. Studies in typically developing children suggest that childhood sleep problems may predict anxiety later in childhood. However, few studies have explored this relationship longitudinally in young children or considered how ASD symptoms may affect these relationships.

Objectives: To examine the influence of early symptoms of ASD on childhood sleep problems and anxiety and the prediction of sleep problems and anxiety from 2- to 8-years of age.

Methods: Data were from the Western Australian Pregnancy Cohort (Raine) Project, which recruited 2900 pregnant women between 1989 and 1991, of whom 2868 were available for follow-up after their child's birth; children were then followed at 1, 2 and 3 years and then every 2-3 years thereafter. Demographic information (108 items) on the mother, father and family at 16-18 weeks gestation was available, and from the 2-year follow-up, information on children's behaviour was collected using the Child Behavior Checklist (CBCL). For the current study the information extracted from the data base included relevant parent and family demographics (13 items), and information on children's sleep, anxiety and ASD symptoms at 2-years and sleep and anxiety at 8-years from CBCL data collected at these ages.

Results: Sleep, anxiety and ASD symptoms at 2-years and sleep and anxiety at 8-years were all significantly correlated. Four hierarchical multiple regressions, two with sleep at 8-years and two with anxiety at 8-years as the dependent variables were conducted. Mothers' and fathers' and family demographics, and the child's gender were entered first into all regressions. For the prediction of sleep at 8-years, sleep and anxiety at 2-years and anxiety at 8-years were entered into the first model, and ASD symptoms at 2-years was added after gender in the second model. For the prediction of anxiety at 8-years, anxiety and sleep at 2-years and sleep at 8-years were entered for the first model and ASD symptoms at 2-years was added after gender in the second model. All final models were significant. Anxiety at 2-years, sleep problems at 2-years and sleep problems at 8-years uniquely predicted anxiety at age 8, and sleep problems at age 2 and anxiety at 8-years uniquely predicted sleep problems at age 8, with each of the 8-year-old variables explaining the most variance. ASD symptoms at 2-years was a unique significant predictor of anxiety at age 8, but not sleep. Two demographic variables also contributed significantly to the prediction of sleep at 8-years.

Conclusions: This study supports research showing that childhood sleep problems and anxiety are interrelated. Children who currently present with either poor sleep or anxiety are likely to experience difficulties with the other. Importantly, early ASD symptoms were related to both poor sleep and anxiety, and contributed significantly to anxiety later in childhood.

**174.078 78** Food Selectivity, Gastriontestinal Dysfunction, BMI Status, and Caregiver Feeding Styles in Children with ASD. K. Strauss*, M. Esposito and L. Fava, *Autism Treatment and Research Center "Una Breccia nel Muro"; Rome, Italy*

Background:

To date research examining food selectivity (FS), gastrointestinal dysfunction (GID) and BMI status lead to inconsistent results, reporting both very high and low levels of co-occuring FS and GID. Furthermore, presence or type of GID and differences from typical BMI growth curves are not necessarily associated to dietary intake. A variety of treatments packages aim to increase diet variety and developing food preferences by teaching parents to apply a variety of strategies from structuring meals, reduction of response effects to antecedent approaches. Nevertheless, limited research exist on feeding practices applied by parent before specific parent training is applied. View available research indicate that parents meet their child's selectivity demands in order to avoid maladaptive behaviors, and that permissive parent feeding styles relate negatively to children's dietary intake. Other research indicate that food selectivity is related to increased risk of obesity

Objectives:

The aim of this cross-sectional study is (1) to examine the association of the presence of GID and atypical BMI percentiles with food selectivity; (2) to specify the role parent feeding style play in this interaction.

Methods:

Fifty children with autism spectrum disorder participated in this study. Diagnostic status was determined based on the DSM-IV, ADI-R, ADOS-G and independently confirmed. Participants were aged 25 to 72 months (mean=50.42, SD=19.22) with 42 (84%) being male. All participants were registered with the Early Intervention Program at the Autism Treatment and Research Centre Una Breccia nel Muro. FS was assessed via the Brief Assessment of Mealtime Behaviors In Children (Hendy et al., 2012), dietary intake, GID and BMI via a survey adapted from Badalyan & Schwartz (2012), as well as the Caregiver's Feeding Style Questionnaire (Hughes et al., 2011).

Results:

Preliminary results confirmed that the majority of participants (~62%) demonstrated differences from typical BMI percentiles with ~54% within overweight and obesity percentile ranges; restricted dietary intakes (~56%) with particularly lacking fruits/vegetables; gastrointestinal problems (~64%) with particularly obstipation; and lastly food selectivity issues (~68%). There was huge variety in parent feeding styles with no obvious pattern present. Detailed analysis that is subject to presentation at the congress is addressed to estimate specifically the relation between GID, BMI, and FS via Analysis of variance (ANOVA). In a second step analysis is adapted with a priori specific contrast (using high demanding/high responsive feeding style as the referent), in order to examine differences in FS, GID and BMI data between the feeding styles. We assumed that in addition to higher use of prompting strategies in parents of children with FS as of those without, there is an additional difference in feeding styles with parents being less demanding in presence of GID, leading to maintenance of selectivity and higher risk of atypical BMI percentiles.

Conclusions:

This study extends previously published work by: evaluating the role of parent feeding styles in the association of FS, GID and atypical BMI percentiles. This in turn, provides information important when evaluating the effectiveness of strategies to promote healthy eating in children with ASD.

**174.079 79** Disorder-Specific and Shared Reward Circuitry Dysfunction in Children with ASD Versus ADHD. G. Kohls*, B. Herpertz-Dahlmann and K. Konrad, *RWTH Aachen Univerity Hospital*

Background: Although attention deficit hyperactivity disorders (ADHD) and autism spectrum disorders (ASD) share certain behavioral, cognitive and neurobiological characteristics, it has been hypothesized to differentiate both disorders based on their brain's reward responsiveness to either social or monetary reward.

Objectives: Thus, the goal of this fMRI study was to differentiate ADHD from ASD on the basis of their brain's reward system reactivity in response to these two types of reward, with greatest differences to be expected for social rewards.

Methods: We investigated the blood-oxygenation-level-dependent (BOLD) effect of both reward types in the context of an incentive go/no-go paradigm in age and IQ-matched boys with ADHD (N=16) versus boys with ASD (N=15) relative to typically developing male controls (TDC, N=17) between the ages of 9 to 18 years.

Results: Task performance and subjective motivation ratings were comparable across all three groups. However, at the neural level a significant group by reward type interaction effect emerged in the ventral striatum with greater activation to monetary versus social reward only in TDC, whereas subjects with ADHD responded equally strong to both reward types, and subjects with ASD showed low striatal reactivity across both reward conditions. Moreover, disorder-specific and shared neural abnormalities during reward processing were revealed, including (a) striatal *hypo*activation in response to monetary reward in ASD relative to TDC and ADHD, (b) orbitofrontal *hyper*activation in response to social reward in ADHD relative to TDC and ASD, and (c) fronto-striato-parietal *hypo*activation in both clinical groups relative to TDC when money was at stake. Interestingly, lower neural reactivity within the fronto-striato-parietal circuitry was associated with higher autistic traits across the entire sample.

Conclusions: In sum, ASD and ADHD are neuropsychiatric disorders with distinct and shared neural dysfunction in response to reward.

**174.080 80** Low Endogenous Fecal Chymotrypsin: A Possible Biomarker for Autism?. M. F. Heil*[1], D. A. Pearson[2] and J. Fallon[1], (1)*Curemark*, (2)*University of Texas Medical School*

Background:

Although there is no approved medication for the treatment of the core symptoms of autism, there may be a subset of children with autism who "self-medicate" by selecting a diet favoring carbohydrates and avoiding protein. These dietary restrictions can be quite marked, and have been hypothesized to be related to oral defensiveness and idiosyncratic behavior. However, it may be the case that at least for a subset of children with autism this self-imposed dietary restriction may reflect a learned association between protein intake and gastrointestinal distress caused by inability to properly digest protein. We hypothesize that this

digestive impairment may reflect a lack of amino acids (e.g., chymotrypsin) that are necessary to digest protein—with undigested proteins becoming allergens that alter gut flora, which in turn may lead to gastrointestinal discomfort. This inability to break down protein into component amino acids may also undermine the synthesis of new proteins such as neurotransmitters, which in turn would ultimately affect cognitive and behavioral status.

Objectives:

The objective of this study was to ascertain whether or not children with autism have abnormally low levels of the enzyme chymotrypsin, a serine protease that cleaves essential amino acids, relative to neurotypical children.

Methods:

Fecal chymotrypsin (FCT) can be reliably measured using fecal samples; a FCT level of <9.0 units/gram is considered abnormally low. Endogenous levels of FCT were compared in 25 children with autism (19 boys; mean CA= 6.5 years) and 31 neurotypical children (15 boys; mean CA= 7.0 years). Children in the autism group met DSM-IV criteria for Autistic Disorder (DSM-IV: 299.00), as screened using the CARS/Gilliam and confirmed using clinical interview. Children in the neurotypical group did not meet DSM-IV criteria for an ASD, as ascertained via clinical. Stool samples were either obtained during a clinic visit or were brought in by the parents, and were tested by Quest Laboratories.

Results:

All children in the autism group had abnormally low FCT (mean FCT=3.96 units/gram; range: 1.2 – 6.4). In contrast, no children in the neurotypical group had abnormally low levels of endogenous FCT (mean FCT =23.7 units/gram; range: 14-35). ANOVA procedures revealed that these group differences were highly significant, $F(1,44)= 227.53$, $p< .0001$. There were no significant effects of age or gender on FCT level. Most notably, given there was no overlap between the two groups in terms of FCT level.

Conclusions:

The results of this initial investigation strongly suggest that there may be at least a subset of children with autism who have very low levels of FCT, in comparison with their typically-developing peers. If this discontinuity in FCT between the two groups is replicated in a larger cohort of children, it may be the case that fecal chymotrypsin (FCT) may have utility as a potential biomarker for at least a subset of children with autism, and that enzymatic replacement therapy to compensate for this low FCT level may be indicated in these children.

**174.081 81** Medical and Behavioral Correlates Associated with a History of Depression in Children and Adolescents with ASD. J. L. Greenlee*, A. S. Mosley, K. Gotham and J. Veenstra-VanderWeele, *Vanderbilt University*

Background: In addition to reports of rising prevalence rates of autism spectrum disorders (ASD) themselves, research suggests that ASD is associated with medical and psychiatric comorbidities at higher rates than are observed in typically developing children. Although coexisting psychiatric problems are often not the focus of treatment, research suggests that they can exacerbate the core symptoms of ASD and negatively impact a child's functionality and quality of life. To this effect, depressive syndromes have been shown to be a particularly common and impairing comorbidity across a range of ages.

Objectives: To identify medical and behavioral problems that are associated with a history of depressive symptomology in ASD.

Methods: A large ASD-only data set ($N$=4098; age 2-17 years, $M$=6.2, $SD$=3.44) from the Autism Treatment Network was divided into two groups based on caregiver endorsement of current or previous diagnoses of depression. Using ANOVA and Chi-square analyses, these groups were compared on several medical and behavioral factors. Dependent variables were operationalized with the Child Behavior Checklist and the 27-item Health and Mental Health History form. .

Results: Bivariate analysis of the data revealed significant differences in the characteristics of the Depressed ($N$=135) and Non-depressed ($N$=3963) groups. The largest effect was age, with the Depressed group being significantly older ($\chi^2$ = 133.13, $p< .001$; Depressed $M$= 11.3 years, $SD$= 3.5; Non-Depressed $M$=6.0 years, $SD$= 3.3). The

Depressed group was also more likely to have Asperger's disorder (30% vs. 7.6% of the Non-Depressed group; $\chi^2 = 19.8$, $p < .001$); or PDD-NOS (20.7% vs. 19.7% of the Non-Depressed group; $\chi^2 = 7.7$, $p = .003$). Average IQ did not differ between groups. After controlling for age and within-spectrum diagnosis, the Depressed group and the Non-Depressed group significantly differed in their report of seizures and seizure disorder ($\chi^2 = 14.6$, $p < .001$), GI problems ($\chi^2 = 25.2$, $p < .001$), history of other psychiatric disorders ($\chi^2 = .27.29$, $p < .001$), and self-injurious behavior and aggression ($\chi^2 = 18.63$, $p < .001$), with the Depressed group displaying these problems at significantly higher percentages. The groups did not differ in reports of family history of depression and other psychiatric problems, eating problems, repetitive behavior, social deficits, or ADHD symptoms. For sleep problems, psychotropic medication use and history of anxiety, the Depressed and Non-Depressed groups differed significantly in the unadjusted model but not after controlling for age and diagnosis.

Conclusions: These findings suggest the existence of ASD subgroup(s) with more complicated and numerous comorbidity, versus a clear "ASD+Depression" group. This should inform studies of both depression mechanisms and treatments in ASD. In addition, the presence of these medical and behavioral problems in individuals with ASD may flag the need to screen for depressive features. Further research is needed to better define the relationship between these comorbidities and depression in ASD.

**174.082 82** Overweight and Obesity in Children with Autism Spectrum Disorders. S. N. Grondhuis* and M. G. Aman, *The Ohio State University*

Background: Childhood overweight and obesity are considerable problems both in the United States and worldwide. Abnormal weight is often accompanied by increased physical and mental health complications including diabetes mellitus, cardiovascular issues, and depression. Elevated body mass in childhood generally leads to overweight in adulthood and is associated higher rates of morbidity and mortality. Youth with intellectual or developmental disabilities, such as autism spectrum disorder (ASD), appear to be at heightened risk for overweight and obesity due to high medication use, atypical eating habits, and sedentary behavior. Previous literature is mixed as to whether these children actually have higher prevalence rates of overweight and obesity, although the methodology of some studies has been subpar due to use of parent-derived height and weight, and small sample sizes.

Objectives: The objective of this project was to reevaluate the prevalence of overweight and obesity for children with ASDs and to compare them to those of typically developing youth. To supplement this information, we also investigated whether there were risk factors associated with abnormal weight.

Methods: Data were acquired through the Autism Treatment Network (ATN) and included children from 17 sites in the United States and Canada. Body Mass Index (BMI) percentiles were calculated according to the Centers for Disease Control and Prevention (CDC) criteria. These were compared to normative samples in other literature. A hierarchical regression was used to determine whether risk factors for abnormal weight could be identified. Variables of interest included demographic information, medications, sleep problems, comorbid psychopathology, cognitive functioning, and ASD subtype.

Results: For the sample of 2,610 subjects, 118 (4.5%) children were underweight, 859 (32.9%) were overweight (exceeding top 15% relative to norms), and 452 (17.3%) were obese (exceeding 5% of normative sample) based on BMI. This means that 1,633 (62.6%) children in the sample had normal weight for their heights. When compared to the existing literature on the typically developing population, neither the rate of overweight nor obesity in children with ASDs was significantly different. When these figures were contrasted with other children with ASD from a previous study, there also were no differences in prevalence of overweight or obesity. Asian heritage, high levels of paternal education, stimulant medication use, atomoxetine use, high scores of the Anxious/Depressed CBCL subscale, and having DSM-IV pervasive developmental disorder–not otherwise specified were associated with lower BMI percentile. Hispanic heritage, SSRI use, alpha 2 agonist use, high scores on the Sleep Disordered Breathing subscale of the Children's Sleep Habits Questionnaire, and elevated scores of the CBCL Aggressive Behavior subscale and Withdrawn/Depressed subscale were associated with higher BMI percentile (greater

likelihood of being overweight or obese), but the amounts of variance explained were very small.

Conclusions: In this sample, children with ASDs were not significantly more likely to be overweight or obese than their typically developing peers, although both groups had nominally higher rates in comparison to the CDC criteria. We also found that the predictors of abnormal weight were similar to typically developing children.

**174.083 83** Psychological Burden on Parents of Children with Autism in Oman. O. A. Al-Farsi*[1], Y. M. Al-Farsi[1], M. I. Waly[1], M. M. Al-Sharbati[1], M. A. al-Shafaee[2], A. Ouhtit[1], M. M. Al-Khaduri[1], M. F. Al-Said[3] and S. al-Adawi[1], (1)*Sultan Qaboos University*, (2)*S.Q.U.*, (3)*Sultan Qaboos university*

**Background:**

Caregivers of children with ASD may be prone to different psychological distress such as stress, depression, grief, fatigue and changes in social relationships. Few studies have attempted to quantify the psychological burden on caregivers manifested as feeling with embarrassment, overload, resentment, isolation from society, and loss of control**.**

**Objectives:**

The aim of this study is to evaluate the severity of psychological burden among parents of children with autism in Oman in comparison to parents of non-ASD children.

**Methods:**

A population-based case-control study was conducted among parents of 122 cases of children with ASD and 122 non-ASD controls. The controls were matched on age, gender, ethnicity, and place of residence. A standardized and validated Arabic version of The Zarit Burden Interview (ZBI-22) has been used to evaluate the level of burden among cases and controls.

**Results:**

Overall, the mean ZBI-22 score of psychological burden among parents of children with ASD was 42.9 (SD = 17.6) which was significantly higher than that among parents of control group (26; SD= 10.8), P-value = 0.04. Among cases, 17% of parents suffered from severe psychological burden compared to none among controls. A substantial proportion of cases (31%) reported moderate psychological burden compared to only 12% among controls, and the difference was statistically significant (P= 0.01). Among cases, mothers reported a higher mean ZBI-22 score compared to fathers (49.7 vs. 35.5), and the proportion of mothers who suffered from severe burden was significantly higher than that among fathers (29% vs. 5%; P-value = 0.001).

**Conclusions:**

The study provides a suggestive evidence that the psychological burden on parents caring for children with ASD is substantial, especially among mothers. The study calls for considering provision of psychological support to parents as an essential component of holistic approach of management of cases of ASD children.

**174.084 84** Relationships Between the Web-Based SNAP-IV and Commercial Measures of Core ADHD Symptoms in Children with ASD. D. A. Pearson*[1], K. A. Loveland[1], M. G. Aman[2], C. W. Santos[1], R. Mansour[1], D. Lane[3], M. M. Nadeau[1], E. W. Shum[1], D. Elledge[1], E. Mitaro[1], A. Shields[1] and L. A. Cleveland[1], (1)*University of Texas Medical School*, (2)*Ohio State University*, (3)*Rice University*

Background:

Clinicians, educators, and researchers have many alternative psychometric measures available to them tapping symptoms of ADHD. With the advent of DSM-5, a diagnosis of ADHD is no longer precluded in a child with ASD—and thus the need for assessment of ADHD in this population will likely rise. Although many commercially available instruments have excellent psychometric characteristics and provide information regarding comorbid conditions (e.g., anxiety), there are circumstances when these instruments are either unavailable (e.g., a parent seeking preliminary information) or when the cost of commercial instruments is prohibitive (e.g., in a rural school district with minimal psychological assessment funding). In these circumstances, a no-cost web-based screen for ADHD would be a helpful first step in determining which children with ASD might warrant a comprehensive follow-up evaluation. What is unknown is how strongly related internet-based and commercial measures of ADHD symptoms are in children with ASD.

Objectives:

The purpose of this study was to compare parent and teacher ratings of ADHD symptoms (e.g., inattention, hyperactivity) on the SNAP-IV [available at www.adhd.net] to parent and teacher ratings of ADHD symptoms on widely used commercial measures of ADHD symptoms.

Methods:

Participants were 77 children (63 boys; mean age=9.3 yrs; mean IQ=86) who met DSM-IV criteria for autism on the ADI-R and the ADOS. Parent ratings on 12 subscales tapping ADHD symptoms on the Conners Parent Rating Scale-Revised (CPRS-R), Child Behavior Checklist (CBCL), Aberrant Behavior Checklist (ABC) and ADD-H Comprehensive Teacher's Rating Scale *(*ACTeRS) were compared to parent ratings on 2 subscales on the SNAP-IV tapping ADHD symptoms, using correlational methods. Similar comparisons were performed for corresponding teacher ratings.

Results:

Significant correlations (all $p<.01$, range: $r=.30$ to $r=82$; average $r=.60$) were obtained between the parent ratings of ADHD symptoms on the SNAP-IV with parent ratings of ADHD on the CPRS-R, CBCL, ABC, and ACTeRS. A similar pattern was seen for teacher ratings (all $p<.01$, range: $r=.27$ to $r=.86$; average $r=.61$).

Conclusions:

These findings indicate that the parent and teacher ADHD ratings on this web-based measure of ADHD are highly correlated with commercial measures of ADHD in school-age children with ASD. Thus, the SNAP-IV, a web-based measure of ADHD symptomatology, would appear to have a helpful role in screening for a comprehensive assessment providing information regarding clinical severity of ADHD symptoms and its commonly comorbid concerns in school-age children with ASD.

**174.085 85** Sleep Quality Among Adolescents with ASD in Relation to Internalizing and Externalizing Symptoms. M. M. Abdullah*, J. N. Phung and W. A. Goldberg, *University of California, Irvine*

Background: Greater than half (66%) of parents report at least moderate sleep problems among their young children with ASD (Souders et al., 2009). Parent reports of diminished sleep quality continue to persist from early childhood into early adolescence among their children with ASD (Humphreys et al., 2013). The majority of studies regarding sleep quality among children with ASD have relied on parent reports. However, recent work that extends the measurement of sleep quality to include self-reports of adolescents with ASD corroborates greater sleep problems as compared to typically developing peers (Baker et al., 2013). The current study adds to the literature by examining emotional and behavioral correlates of self-reported sleep quality among adolescents with ASD.

Objectives: To examine the associations between self-reported sleep quality of adolescents with ASD and their (1) self-reported internalizing symptoms, and (2) parent-reported internalizing and externalizing symptoms.

Methods: Participants were 31 adolescents who had been clinically diagnosed with ASD and their mothers. Adolescents were between 12 and 18 years, predominantly male (90%), and were within average intellectual functioning. Adolescents and their mothers completed questionnaires during study home visits. Sleep quality was measured with the School Sleep Habits Survey (SSHS; Wolfson & Carskadon, 1998), an adolescent self-report with two subscales: (1) the Sleepiness Scale and (2) the Sleep/Wake Problems Behavior Scale. Internalizing and externalizing symptoms were measured using both adolescent and parent questionnaires. Two adolescent self-reports of internalizing symptoms were used: (1) the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1991) for depressive symptoms and (2) the Multidimensional Anxiety Scale for Children (MASC; March, 1997) for anxious symptoms. Parent reports of adolescent internalizing and externalizing symptoms were measured using the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001).

Results: Adolescent reports of greater sleepiness were significantly linked to adolescent reports of greater depressive symptoms ($r=.502$, $p=.004$) and anxious symptoms ($r=.531$, $p=.002$). Similarly, adolescent reports of greater sleep/wake problems were significantly related to adolescent reports of greater depressive symptoms ($r=.413$, $p=.023$) and greater anxious symptoms ($r=.374$, $p=.042$). In contrast, adolescent reports of sleepiness were not

associated with parent reports of adolescent internalizing symptoms. Whereas adolescent reports of greater sleepiness were significantly linked to parent reports of adolescent externalizing symptoms ($r$=.462; $p$=.009), adolescent reports of sleep/wake problems were not related to parent reports of adolescent externalizing symptoms.

Conclusions: Poor quality sleep is a common problem for adolescents with ASD. This study extends previous work by examining self-reported sleep quality in relation to self- and parent reports of internalizing and externalizing symptoms among adolescents with ASD. Results show that more sleep problems are linked to self-reports of more internalizing symptoms and parent reports of more adolescent externalizing symptoms. Differential associations between sleep problems and both self-reported internalizing and parent-reported adolescent externalizing symptoms have clinical implications regarding respondent variability. These findings underscore the importance of obtaining the perspectives of both adolescents with ASD and their parents during evaluations of adolescent sleep, emotional, and behavioral symptomatology, as well as when evaluating responses to interventions directed toward these domains.

**174.086 86** Sleep and Executive Functioning Among High-IQ School-Aged Children with Autism. N. Nayudu*, G. Greco, C. Sonners and S. Faja, *University of Washington*

Background: Among typically developing children sleep has been related to executive function (e.g., Karpinski et al., 2008; Beebe et al., 2004) and sleep disorders are more common among children with autism spectrum disorders (ASD) (Humphreys et al., 2013). To our knowledge, there have been no published investigations of sleep and executive control in children with ASD.

Objectives: To test whether young, high-IQ children with ASD differ from typically developing comparison children in parent reported sleep duration and sleep problems, and to test whether sleep is related to executive function among children with ASD.

Methods: Data collection is ongoing. To date, 34 6- to 11-year-olds with ASD and 36 age-matched controls participated. All children had cognitive ability in the average or above average range. Parent report of sleep was measured via the Child's Sleep Habits Questionnaire (CSHQ; Owens et al., 2000) for 40 children. Sleep duration was collected from an additional 30 children who completed the executive function battery. The executive function battery included the Backward Digit Span and Stroop tasks, and parent report via the Behavioral Rating Inventory of Executive Function (BRIEF).

Results: Preliminary results suggest children with ASD had greater sleep-related anxiety, $t(38) = 2.52$, $p < .001$, night waking, $t(38) = 1.33$, $p = .01$, parasomnias, $t(38) = 2.48$, $p = .02$, sleep-disordered breathing, $t(38) = 1.25$, $p < .01$ and daytime sleepiness, $t(38) = 3.42$, $p = .02$. Scores on sleep duration, bedtime resistance, and sleep onset delay did not differ. Among the group with ASD, children who slept less had more parent-reported difficulty regulating their behavior, $r(34)= -.38$, $p = .03$. Children with higher levels of bedtime resistance had more executive dysfunction, $r(16)= .53$, $p = .03$, and difficulties with behavioral regulation, $r(16)= .63$, $p < .01$. Children with ASD who had reduced sleep duration had more executive difficulties, $r(16)= -.77$, $p < .001$, behavioral dysregulation, $r(16)= -.71$, $p < .01$, and difficulty with metacognition, $r(16)= -.62$, $p = .01$. Children with reduced sleep onset delays had better working memory ability on the backward digit span, $r(15)= -.54$, $p < .04$. During the Stroop task, children who had more night waking had reduced accuracy, $r(11)= -.71$, $p = .01$ and slower response times, $r(11)= .68$, $p = .02$, during the conflict condition.

Conclusions: Consistent with previous findings, compared to typically developing children, young school-aged children with ASD and IQ in the average range or above had higher levels of parent-reported sleep-related anxiety, night waking, parasomnias, sleep disordered breathing, and daytime sleepiness. Within the group with ASD, sleep duration and resistance to falling asleep related to parent report of behavioral regulation and executive dysfunction. Performance on working memory and inhibition tasks also corresponded with sleep. The ability to fall asleep quickly corresponded with better working memory, whereas the ability to remain asleep through the night corresponded with better accuracy and efficiency inhibiting conflicting information. These preliminary results suggest that more investigation is needed to understand

how sleep disruptions are related to poor executive function in children with ASD.

**174.087 87** Specific Hypolipidemia Caused By VLDL Lipolysis in Children with ASD. H. Matsuzaki*[1], K. Iwata[1], K. Nakamura[2], M. Tsujii[3] and N. Mori[4], (1)*University of Fukui*, (2)*Hirosaki University*, (3)*Chukyo University*, (4)*Hamamatsu University School of Medicine*

Background:

The neurobiological basis for autism remains poorly understood, but evidence is mounting in support of lipid metabolism playing a role in autism spectrum disorder (ASD). We have already revealed that Very Low Density Lipoprotein (VLDL) triglyceride was significantly decreased in children with ASD than those of normal control subjects (US PATENT #8518659). To elucidate the mechanism of VLDL down-regulation, it was necessary to clarify whether VLDL was reduced due to activation of the degradation or inhibition of its synthesis.

Objectives:

In order to clarify the mechanism of VLDL down-regulation in ASD, we carried out measurements of free metabolite in plasma of children with ASD and examined correlation between VLDL triglyceride and the metabolites detected.

Methods:

This study enrolled 30 children (6-11yrs old) with ASD recruited from the Asperger Society Japan and 30 age-matched healthy control subjects recruited by advertisement. Fasting human blood samples were collected by venipuncture in a sitting position with a tourniquet from all participants for both groups who are Japanese and drug-naïve. LC/CE-TOFMS measurement of free metabolite in the plasma was carried out using an Agilent LC System and CE Capillary Electrophoresis System (Agilent Technologies, Waldbronn, Germany). The size distribution of plasma lipoprotein particles was evaluated by high sensitivity lipoprotein profiling system with high-performance liquid chromatography (Skylight Biotech, Inc., Akita, Japan).

Results: By TOFMS analysis, a total of 258 metabolites were detected in the plasma of all set. Of these, 83 metabolites showed significantly different relative areas between the ASD children and the controls ($p<0.05$). The present study identified deviated plasma metabolite levels associated with oxidative stress and mitochondrial dysfunction in children with ASD. More, we found significant correlation between VLDL triglyceride decrease and 20 metabolites change including 12 free fatty acids, 3 free acylcarnitines, alanine, loganin, 2-hydroxybutyric acid, 3-hydroxybutyric acid and O-acetylcarnitine (ALCAR) in the ASD participants ($p<0.05$). Of these 20 metabolites, Alanine and Loganin were lower but the others were higher in the ASD participants than controls.

Conclusions:

These results suggested that VLDL-specific lipolysis due to aberrant b-activation of fatty acid via oxidative stress and mitochondrial dysfunction may cause VLDL triglyceride decrease in plasma of children with ASD. VLDL triglyceride in peripheral blood might be surrogate marker implicated in oxidative stress and mitochondrial dysfunction in ASD.

**174.088 88** Stress, Anxiety, and Depression Among Parents of Children with Autism in Oman: A Case-Control Study. O. A. Al-Farsi*[1], Y. M. Al-Farsi[1], M. I. Waly[1], M. M. Al-Sharbati[1], M. A. al-Shafaee[2], A. Ouhtit[1], M. M. Al-Khaduri[1], M. F. Al-Said[3] and S. Al-Adawi[1], (1)*Sultan Qaboos University*, (2)*S.Q.U.*, (3)*Sultan Qaboos university*

**Background:**

There is an increasing evidence supporting the notion that caregivers of children with autism spectrum disorders (ASD) suffer from increased risk of psychological disturbances. Nonetheless, results are not consistent with regard to prevalence rates and types of psychological disturbances. In particular, the evidence exploring this topic among Arab communities is almost lacking.

**Objectives:**

To describe patterns of stress, depression, and anxiety among parents of children with ASD among an Arab population in Oman, compared to parents of non-ASD children.

**Methods:**

A population-based case-control study has been conducted on 122 parents of ASD children and two control groups: 90parents of typically-developed children(TD group) and 81 parents of children suffer from intellectual disabilities other

than ASD (ID group). Stress, anxiety, and depression among study groups have been assessed using a validated and standardized Arabic version of The Depression Anxiety and Stress Scale (DASS-21).

**Results:**

Overall, the proportion of parents of children with ASD who suffer from stress was 46%, which was higher than that reported among parents of TD group (33%) and ID group (37%). The difference was statistically significant (P-value 0.04). Compared to control groups, parents of ASD group who suffer from anxiety were proportionately higher (43% vs. 26% and 25%) and the difference was statistically significant (P-value 0.001). Similar pattern was also observed in terms of reported depression (70% vs. 35% and 36%) and the difference was statistically significant (P-value 0.02). The mean score of stress, depression and anxiety have been significantly greater among parents with ASD compared to parents with intellectual disabilities, and typically developing children.

**Conclusions:**

The study provides suggestive evidence of increased risk of stress, anxiety, and depression among parents of ASD children compared to parents of children who are free of ASD. It calls for giving more emphasis to the psychological well-being of parents of ASD children.

**174.089 89** The Childhood Autism Spectrum Test (CAST) As a Screener for High-Functioning Children, Adolescents, and Young Adults with Autism Spectrum Disorder. T. Gev*[1], I. Grinvald[2] and O. Golan[2], (1)*The Association for Children at Risk*, (2)*Bar-Ilan University*

Background: Screening older children, adolescents, and adults for an Autism Spectrum Disorder (ASD) diagnosis may be challenging, due to characteristics being masked by learned strategies, as well as the existence of psychiatric co-morbidities. Therefore, the use of a screener examining the existence of diagnostic features at an earlier age, when these are more crystalized, may assist in referring relevant applicants for a thorough diagnostic assessment.

This study evaluated The Childhood Autism Spectrum Test (CAST, Scott et al., 2002), as a parent-report screener with children in the age group it was originally designed for (6-11), as well as with adolescents (aged 12-17) and adults (aged 18-46), whose parents were asked to report on their behavior during primary school years.

Objectives: To evaluate the stability of the CAST as a screener in three age groups, and to report on its psychometric properties in an Israeli sample.

Methods: Parents of 43 individuals (15 children, 11 adolescents,17 adults), who were diagnosed with ASD by professional clinicians using the ADI-R (Lord et al., 1994) and the ADOS-G (Lord et al., 2000), filled out the CAST as part of their assessment process at an ASD clinic. In addition, a group of 101 parents of individuals from the general population (parents of 35 children, 30 adolescents and 36 adults) matched on child's age and gender filled out the CAST electronically.

Results: the clinical group scored significantly higher on the CAST (M=17.04, SD=5.93), compared to the general population group (M=6.18, SD=4.02), with no significant differences between age groups and no diagnosis by age-group interaction. A cutoff score of 13, two points lower than the original cutoff (Scott et. al., 2002) yielded sensitivity of 0.84 and specificity of 0.86. Internal consistency for the CAST was α=0.9, with sub-scales' internal consistency ranging between 0.63-0.79. Discriminant analysis revealed the accuracy of prediction using all CAST items was 90%. In addition, the CAST distinguished between participants diagnosed with ASD and participants in the general-population group, whose parents reported they have an ADHD diagnosis.

Conclusions: Parental report on childhood behavior using the CAST may serve as a good screener for children, as well as for adolescents and adults with ASD. Our preliminary results also suggest the CAST discriminates well between individuals with ASD and those with ADHD. This finding may be of importance due to diagnostic overlaps between the two conditions in higher-functioning individuals.

**174.090 90** The Developmental Clinical Instrument (DCI): Structured Data Collection for the Autism-Focused Clinical Exam. D. Grodberg*[1], P. M. Weinger[2], L. Bush[2] and A. Kolevzon[2], (1)*Mount Sinai School of Medicine*, (2)*Icahn School of Medicine at Mount Sinai*

Background: Gold standard research diagnostic criteria for ASD includes meeting threshold criteria on the ADOS and ADI-R, confirmed with a clinical examination guided by DSM-5 diagnostic criteria. Such rigorous diagnostic characterization of research subjects is intended to standardize case ascertainment.

Yet, despite high fidelity use of the ADOS and ADI-R, case-ascertained ASD samples continue to possess heterogeneity due to a myriad of physical, medical and psychological conditions inherent to the disorder. Such heterogeneity varies within and across study populations and can influence effectiveness research, outcomes research, and cost-effectiveness research.

The clinical examination provides an opportunity to recognize such phenotypic variability. But clinical exam data typically resides in unstructured free text forms. This prevents systematic collection of comparable data and as a result, a wealth of information reflecting physical, medical and psychological conditions within and across groups of patients remains underutilized.

We developed the Developmental Clinical Instrument (DCI), which standardizes the documentation of an autism-focused clinical examination. The DCI does not change a physician's behaviors; it simply structures data collection. Importantly, the DCI contains embedded quantitative data elements that can facilitate entry into an online data capture system. Use of the DCI and its embedded data elements can reduce the time and cost of data collection, improve data quality, facilitate data sharing and improve opportunities for meta-analysis and comparison of data across different sites and clinical populations. The DCI also has a customizable section for additional study-specific data elements.

Objectives: To implement the DCI at an autism research center as a means of standardizing the collection of embedded data elements and to facilitate the rapid generation of cross sectional data for specific data elements in our study population.

Methods: The DCI was used to structure documentation of study physicians' clinical examination at the Seaver Autism Center for Research and Treatment. The clinical examination is one part of the IRB approved assessment protocol that also includes the ADOS, ADI-R, and other cognitive and adaptive measures. The data elements contained in each DCI of 20 consecutive research subjects were entered into a customized data collection system that generates real time analyses. Reports were rapidly generated to reflect cross sectional data.

Results: Clinician buy-in and compliance with the DCI was high. In this population of research subjects, cross sectional data reflecting the distribution of each data element contained in the medical history of the DCI was generated. A chart reflecting this data is displayed in figure 1.

Conclusions: The DCI facilitates structured data collection for the autism-focused clinical examination. When used with a customized data capture system, the DCI can facilitate the generation of reports that display distributions of specific data elements within a population. Furthermore, structured data collection of physical, medical and psychological data can lay the foundation for multivariate or case control analyses to support hypothesis generation. Finally, use of the DCI in non-research clinical settings can lay the foundation for epidemiologic surveillance of data elements in populations not typically exposed to research.

**174.091 91** The Influence of Gender and Age on Prevalence Rates of Comorbid Disorders in Autism. K. Supekar*, T. P. Iyer, P. Odriozola and V. Menon, *Stanford University*

**Background:**

Individuals diagnosed with autism spectrum disorder (ASD) frequently suffer from one or more other disorders. Yet, despite the obvious need to assess the prevalence rates of such comorbidities, few studies have attempted more than a cursory analysis of these across the ASD population.

**Objectives:**

In this study, we attempt to fill in the gaps in existing studies of ASD comorbidity by examining the influence of gender and age - two important, yet understudied, factors - on ASD comorbidities.

**Methods:**

We conduct a comprehensive statistical examination of ten ASD comorbidities including attention deficit hyperactivity disorder (ADHD),

autoimmune disorder, bowel disorders, CNS/cranial anomalies, diabetes mellitus, epilepsy, inflammatory bowel disorders, muscular dystrophy, schizophrenia, and sleep disorders by analyzing clinical data of over a million individuals who were patients of the Stanford University Medical Center.

**Results:**

We found significantly higher proportions of ADHD, autoimmune disorders, bowel disorders, CNS/cranial anomalies, epilepsy, and schizophrenia in the ASD population compared to the non-ASD population; illustrating higher susceptibility of individuals on the spectrum to these comorbidities. Critically, there was a lower male bias in comorbidity rates in the ASD than in the non-ASD population; i.e., all ten disorders showed significantly higher prevalence rates in males than females in the non-ASD population whereas the ASD group showed more variation by gender. Additionally, the ASD sample exhibited a more variable trajectory of comorbidity rates with age than did the non-ASD sample. Epilepsy, for example, decreased from a staggering 41.12% in ages 0-18 down to 24.43% and 15.15% in ages 18-35 and ages 35 and above, respectively; while remaining at a relatively consistent .8 - 1.8% in the non-ASD sample. The observed gender differences varied with age in both groups, but these fluctuations were more dramatic in the ASD population. Notably, the prevalence of bowel disorders was highest in males in both the 0-18 and the 18-35 age range, then switching to higher prevalence in females in ages 35 and above. Similarly, schizophrenia was more prevalent in males 0-18 years of age, but then had higher rates in females in the 18-35 and 35 and above age ranges.

**Conclusions:**

Our results, obtained from comprehensive analyses of one of the largest clinical cohort to date, highlight crucial and unique differences between patterns of comorbidities and their interactions with gender, age, and ASD diagnosis. These findings may prove to be instrumental in developing more efficient gender- and age-appropriate diagnostic and treatment strategies for ASD and related disorders. More generally, our study highlights the importance of understanding and accurately identifying patterns of comorbidity in the ever-growing ASD population as these co-occurring problems mediate the degree of adaptation, lifestyle, and prognosis of individuals on the spectrum.

**174.092 92** Uncovering Sex-Steroid Related Conditions in Women with Autism: A Latent Class Analysis. A. Pohl*[1], B. Auyeung[2], S. A. Cassidy[1] and S. Baron-Cohen[2], (1)*Autism Research Centre, Department of Psychiatry, University of Cambridge*, (2)*University of Cambridge*

Background: Elevated levels of prenatal androgens, such as testosterone (T), during a critical period are hypothesized to contribute to the etiology of autism spectrum conditions (ASC), as fetal T shapes neurological development. Prenatal androgens also contribute to the programming of the hypothalamic-pituitary-gonadal (HPG) axis. In females, elevated levels of prenatal androgens also contribute to the etiology of polycystic ovary syndrome (PCOS). Following an earlier study in 2007, the present study further explores the link between ASC, HPG programming, and PCOS in a larger sample of women.

Objectives: (1) To test if elevated rates of sex steroid-related symptoms and conditions in women with ASC replicate in a larger sample; and (2) to assess sex steroid-related symptom patterns within women with ASC and controls.

Methods: We tested 2 groups of women, screened using the Autism Spectrum Quotient (AQ): Group 1: n=415 women with ASC (mean age (standard deviation) 36.39 (±11.98) years); Group 2: n=415 controls (mean age (standard deviation) 39.96 (±11.92) years). All participants completed the Testosterone-related Medical Questionnaire (TMQ) online, which was designed to measure steroid-related symptoms and conditions. Fisher's Exact Test was used to assess group differences in reported rates of steroid-related symptoms. We assumed that response patterns on the TMQ reflect underlying steroid circulation and sensitivity, and a multiple-group latent class analysis (LCA) was used to identify differences in latent class structure between women with ASC and controls.

Results: We confirmed significantly higher frequencies in females with ASC of (1) sex steroid-related medical conditions: epilepsy ($p=0.016$), amenorrhea ($p=0.0002$), dysmenorrhea ($p<0.0001$), severe acne

[contraceptive pill users (p=0.053), non-users (p=0.002)] and anorexia (p<0.0001); (2) non-heterotypical gender identity and sexual orientation, related to fetal testosterone: gender dysphoria (p=0.0004), transsexualism (p=0.030), and differences in sexual preference ($X^2$; p<0.001); and (3) sex steroid-related developmental changes: precocious puberty (p=0.003), and early growth spurt (p=0.002). We conducted a multi-group LCA on 11 items linked to sex steroids, comparing women with ASC to controls. In both groups, two latent classes (typical and 'steroidopathic') emerged. A significantly higher percentage of women with ASC than controls fell into the steroidopathic class characterized by higher posterior probabilities for each steroid-related condition ($\Delta G^2$=15, *df*=1, p=0.0001).

Conclusions: Increased exposure to prenatal androgens atypically programs the HPG axis, resulting in conditions such as amenorrhea, early or late menarche, and hirsutism. We found that adult women with autism reported higher rates of such sex steroid-related conditions than controls. Increased reports of sex-steroid related conditions in women with ASC are consistent with the hypothesis of elevated fetal testosterone in the development of ASC.

## 175 Molecular and Cellular Biology

**175.093 93** A Metabolic Profile of Autism Spectrum Disorder from Autism Phenome Project Patient Plasma. R. Burrier*[1], D. G. Amaral[2], P. West[1], S. J. Rogers[3], A. M. Smith[1], D. D. Li[2], M. Ross[1], B. Fontaine[1] and E. Donley[1], (1)*Stemina Biomarker Discovery*, (2)*University of California Davis Medical Center*, (3)*UC Davis MIND Institute*

Background:

Diagnosis of autism spectrum disorder (ASD) at an early age is important for initiating effective intervention. The current average age of diagnosis in the United States is 4.5 years. Patients can be reliably diagnosed through behavioral testing at 2 years of age only at health care facilities with sufficient autism expertise. Increasing evidence indicates that ASD is a complex disorder that has many causes and a variety of genetic risks. Identification of a metabolic signature of autism from blood samples will offer earlier screening and diagnosis to improve both therapy and outcome.

Objectives:

Stemina has recently completed a study of 4 to 6 year old patients in which a metabolic signature was observed in the patients' blood. We are continuing to perform analysis on blood from patients enrolled in the Autism Phenome Project (APP) to evaluate the metabolic signature of 2 to 4 year old children with ASD as compared to typically developing (TD) children. This research will develop and validate biomarkers associated with ASD discovered in the first study as well as identify new biomarkers in the younger patient cohort that may allow for earlier diagnosis. Our goal is to determine the relevant biomarkers capable of being translated into a broadly available diagnostic test for ASD.

Methods:

Plasma was obtained from 180 children with ASD and from 93 age-matched TD children enrolled in the APP. All subjects were between approximately 2 and 4 years old. Samples were analyzed using 4 different LC/MS-based methods designed to orthogonally measure a broad range of metabolite molecular classes in plasma. Univariate, multivariate and machine learning methods are being used to identify if a predictive metabolic signature exists that is capable of classifying patient plasma samples as being from ASD or TD children. Results from this study will also be compared to the previous study with 4-6 year old children to assess the effect of age on metabolic biomarkers of ASD.

Results:

In the initial study, statistical models were created using 179 statistically significant mass features that classified the ASD and TD samples with an average accuracy of 81%. Metabolites that were altered in children with ASD are derived from multiple biochemical pathways and included organic acids, amino acids, phospholipids and others. This presentation will provide a summary of metabolic signatures identified in the APP cohort; analyses are currently underway.

Conclusions:

The non-targeted, mass spectrometry-based metabolomic analysis of metabolites in plasma shows promise for discovery of metabolic signatures able to differentiate individuals with ASD from TD individuals. These results form the

basis for additional work with the goals of 1) developing a diagnostic test to detect ASD in children to improve patient outcomes, 2) gaining new knowledge of biochemical mechanisms involved in ASD 3) identifying biomolecular targets for new modes of therapy, and 4) identifying biomarkers that can be used for personalized treatment and classification of potential responders versus non-responders through metabolomic analysis of a patient's biochemistry.

**175.094 94** A Microbead-Based Multiplex Immunoassay to Measure Dynamic Protein Interaciton Networks at the Glutamate Synapse. S. E. Smith*[1], S. C. Neier[1], T. R. Davis[1], C. Neuhauser[2] and A. G. Schrum[1], (1)*Mayo Clinic*, (2)*University of Minnesota Rochester*

**Background:** Protein-protein interaction (PPI) networks are thought to represent a system with emergent network properties, integrating signals from a variety of inputs into coordinated responses. At the glutamatergic synapse, interacting networks of proteins, consisting of structural proteins, membrane channels, kinases, ubiquitin ligases and regulatory proteins influence action potential generation and cell fate decisions, including synapse development, maintenance and elimination. Many of these proteins are associated with autism, leading to the current "synaptic hypothesis of autism". Current technology allows the detailed study of individual members of this synaptic interaction network, but network-scale activity of protein-protein interactions, both at rest and following signaling, is incompletely understood.

**Objectives:** To develop a technique to quantitatively measure protein-protein interactions at the network level, and to quantify how these networks change in response to biological signaling events and autism-linked gene mutations.

**Methods:** We have developed a technique called multiplex immunoprecipitation detected by flow cytometry (mIP-FCM). In mIP-FCM, protein complexes are immunoprecipitated onto Luminex microspheres conjugated to antibodies specific for 20+ different proteins, then probed with fluorophore-conjugated antibodies to the same protein set and read on a flow cytometer. In total, 400+ protein-protein interactions are assessed, producing a network-scale analysis of protein interactome dynamics. Our group uses mIP-FCM to study the signaling networks engaged in response to agonist vs. antagonist stimuli of either the T cell immunologic synapse or the neuronal glutamatergic synapse. Here, we present a new mIP-FCM array focused on autism-linked proteins from the glutamate synapse.

**Results:** Using the well-characterized T cell immunologic synapse that forms between a T cell and an antigen presenting cell as a model system, mIP-FCM is capable of assessing 400+ dynamic interactions during a T cell signaling event. We have developed high-sensitivity statistical methods capable of identifying small changes in protein interactions, and visualization methods to make sense of the vast amount of data collected (~7000+ data points per timepoint). Analysis of proteins from the T cell synapse has revealed new network protein interaction patterns that could be decisive in agonist vs. antagonist signal transduction. In our new mIP-FCM array focused on the glutamate synapse, we have targeted 25 autism-related proteins that form a highly interconnected protein interaction network. Our preliminary data focuses on detecting changes in the interaction network specific to excitation or inhibition of synaptic activity.

**Conclusions:** Our goal is to better understand the network-scale alterations in protein-protein interactions during glutamatergic signaling, and how different autism-associated risk factors may play important, perhaps convergent, roles in these synaptic network processes. The data presented here are an important first step towards this goal.

**175.095 95** Effects of Ultrasounds on Human Neuron Connectivity and Microglia Activation: Potential for the Therapeutic Use of Transcranial Ultrasonography in Autism. M. Ruggiero*[1], S. Pacini[1] and J. J. Bradstreet[2], (1)*University of Firenze*, (2)*Brain Treatment Center*

Background:

We and others demonstrated that non-thermal ultrasounds (US) used for diagnostic imaging in transcranial ultrasonography (TUS), improve mental states, reduce chronic pain and anxiety, modulate neurotransmission, and have positive effects on heart frequency, blood pressure and muscle strength (Brain Stimul. 2013 May;6(3):409-15. Neuropsychobiology. 2012;65(3):153-60. The Journal of IiME, vol. 6 (1), p 23-28, 2012). Therefore, it can be hypothesized that TUS might be useful in the

treatment of some of the most disturbing symptoms of autism. However, the precise mechanism of action of US on neurons and microglia cells has not been elucidated as yet.

Objectives:

We decided to treat human neurons and microglia cells in culture with US identical to those used in TUS, and to evaluate whether the changes observed *in vitro* were consistent with the observations reported *in vivo*.

Methods:

Human neuronal cells SH-SY5Y, and microglia cells were obtained from the Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia-Romagna, Brescia, Italy. Cells were routinely maintained at 37°C in a humidified atmosphere of 5% $CO_2$ in Eagle's minimum essential medium in Earle's Balanced salt solution (45%), Ham's F12 medium (45%), foetal bovine serum (FBS) 10%. Cells were treated with US using an Esaote MyLabFive system. A linear probe for TUS was applied onto the Petri dishes for 1 min after having assessed that US were able to cross the plastic well and penetrate the cell monolayer. Immediately thereafter, living cells were observed by phase contrast microscopy without any type of fixation or staining.

Results:

After 1 min US treatment, a significant change in neuronal cell morphology and cell-to-cell connectivity could be observed. US-treated neurons showed a more elongated shape; numerous cytoplasmic bridges between cells could be observed. The increase in neuronal connectivity could be clearly appreciated in those naked areas of the well where thin cytoplasmic elongations connected distant cells. The number of such connections was greatly increased in US-treated neurons. Untreated microglia cells in culture were constantly activated by the presence of serum, and showed the typical round shape that is observed in pathologic, pro-inflammatory microglia activation. After 1 min US treatment, however, microglia cells reverted to the so called ramified state that indicates quiescence and is associated with the lack of production of neurotoxic factors and pro-inflammatory signaling molecules.

Conclusions:

Although TUS is not yet part of autism therapeutic protocols, its effectiveness in areas such as neurological/psychiatric intervention, long-term alertness/wakefulness, behavioural reinforcement, anxiety/stress reduction, cognitive enhancement and pain intervention, suggests that it might be useful in autism treatment as well. Since decreased neuronal connectivity and microglia activation are common neuro-pathological findings in autism (PLoS One. 2013 Jun 18;8(6):e67329), our results demonstrate that the observed effects of TUS can be ascribed to restoration of neuronal connectivity and inhibition of pro-inflammatory microglia activation.

**175.096 96** Gene Expression Deficits in Pyramidal Neurons from the Anterior Cingulate Cortex in Males with Autism. M. J. Chandley*, J. D. Crawford, A. Szebeni, K. Szebeni, J. L. Crawford and G. A. Ordway, *Academic, East Tennessee State University*

Background: Altered brain morphology was one of the first pathobiological findings associated with autism spectrum disorder. These gross abnormalities, documented in both white and gray matter areas in autistic brains, are postulated to contribute to disrupted neuronal communication. For example, glutamatergic pyramidal neurons in the anterior cingulate cortex (ACC) have decreased size and increased cell density in autism.

Objectives: We sought to determine whether autism-related gene expression abnormalities exist in the ACC that might underlie previously observed cell morphological alterations found in this brain region. Specifically, levels of expression of genes associated with glutamatergic neurotransmission were measured in pyramidal neurons and surrounding astrocytes in the ACC of postmortem brain tissues from autism donors and matched developmentally normal control donors.

Methods: Postmortem brain tissues were obtained from 6-8 age-matched pairs of male subjects who had autism and developmentally normal control males (age range 6-37). Laser-guided microdissection was used to capture pure populations of pyramidal neurons and astrocytes from layer III of the ACC. The expression of glutamate-related genes was measured in RNA isolates by reverse transcription followed by end-

point PCR using three stable reference genes to normalize expression levels.

Results: ACC pyramidal neurons from autism subjects demonstrated significantly reduced gene expressions of the obligatory glutamatergic NMDA receptor subunit NR1, a glutamate transporter SLC1A1, and the glutamate receptor anchoring protein GRIP1. There was also a robust reduction in the gene expression of the brain-derived neurotrophic factor (BDNF) receptor NTRK2 in autism pyramidal neurons, with gene expression levels of BDNF itself unaffected. No gene expression abnormalities were observed in ACC astrocytes surrounding the pyramidal neurons from autistic subjects.

Conclusions: Autism spectrum disorder is associated with a reduction in the expression of genes associated with glutamatergic neurotransmission and downstream BDNF signaling in pyramidal neurons of the ACC. These findings suggest that glutamatergic signaling is compromised in these excitatory neurons in autism and raise hope that drugs or other treatments may be developed to overcome these pathobiological deficits.

**175.097 97** Immunological Disarrangements in ASD Are Associated with Biological Processes and Homeostatic Mechanisms in ASD Rather Than Autoimmunity or Pathogenic Inflammation.
C. A. Pardo*[1], A. Thurm[2], C. Farmer[3] and S. E. Swedo[4], (1)*Johns Hopkins University School of Medicine*, (2)*National Institutes of Health - National Institute of Mental Health*, (3)*NIH*, (4)*NIMH*

Background: Interactions between the immune and central nervous system (CNS) are critical for maintenance of homeostasis and brain functions, including cognition. Immunological mechanisms have been hypothesized to play a role in the etiopathogenesis of autism spectrum disorder (ASD), based on observations of abnormalities in a variety of immune markers in serum samples or post-mortem tissues.

Objectives: To establish the immunological profiles in blood and cerebrospinal fluid (CSF) samples from pediatric subjects with ASD, in comparison with blood samples from typically developing children (TYP) in order to evaluate a pathogenic role of observed between-group differences and specific patterns.

Methods: A longitudinal study of clinical and immunological factors associated with ASD was carried out at the NIMH intramural program.106 subjects with autism (mean age 50.4±15.88 months) and 70 typically developing controls (mean age 38.53±15.34 months) were recruited for the study. Autism was diagnosed using the ADI-R and ADOS as well as clinical judgment. Regression history was also assessed using the Regression Validation Interview. Regression was defined as language loss and/or loss of social engagement. Blood and CSF were used to assess the immunological profile in subjects with autism while only blood was analyzed in typical developing controls. Studies to characterize patterns of immune activation and inflammation by flow cytometry, cytokine/chemokine profiling and microbial translocation were carried out.

Results:

- Although there was a significant increase in blood NK cells between ASD and controls, no evidence of activation of immune cells or dysregulation of T-regulatory cells was observed in ASD.
- Abnormally elevated levels of immune mediators such as CD40 ligand (CD40L) and epidermal growth factor (EGF) were found in blood of ASD patients while classical mediators of inflammation such as TNFa, IL6 and other cytokines were similar between ASD and control subjects.
- Cytokine/chemokine profiles in blood and CSF samples were clearly distinct, a result that suggests blood inflammation biomarkers are not suitable markers for assessment of CNS abnormalities in ASD.
- CSF cytokine/chemokine profiles demonstrated increases in monocyte-related mediators such as CX3CL1 (fractalkine), CCL2 (MCP-1) and FLT3-L, a finding that support the view that inductors of microglia activation are dominant in CSF of ASD subjects.

Conclusions: Our studies suggest that immunological abnormalities exist in ASD, but most appear to be related to genetic and environmental factors unrelated to autistic symptomatology. Evidence for a primary

pathogenic role of immune dysfunction was generally absent in this cohort of young children with ASD.

**175.098 98** Low Maternal Progesterone and Autism. P. M. Whitaker-Azmitia*, D. Jenkins and H. D. Garman, *Stony Brook University*

**Background:**

Increasingly**,** researchers have hypothesized that maternal environment could be as important, if not more important, than genetics as a factor contributing to autism. For over 30 years, studies have shown an increased autism risk among children born to mothers experiencing obstetrical complications. Although this is usually interpreted as suggesting that the obstetrical complications could be causing autism, it is equally likely that a single factor could be responsible for both complications and autism. We are proposing that this factor is low maternal progesterone.

Progesterone is not only necessary for a healthy pregnancy; it is also a brain developmental factor, important for myelination, dendritic development, neurogenesis and development of the serotonergic neurotransmitter system. Importantly to our hypothesis, progesterone available to the developing fetal brain is only that which is supplied by the mother.

**Objectives :**

We proposed to test our hypothesis that low levels of the hormone progesterone are responsible for some cases of autism, by determining the number of progesterone-related obstetrical events in mothers of autistic children.

**Methods:**

In order to test this hypothesis, we conducted a survey of mothers of autistic children (n=86) compared to mothers of typically-developing children (n=88) regarding obstetrical histories, including five obstetrical events indicative of low progesterone: contraceptive failure, excess weight gain, vaginal bleeding, fertility treatments and low fertility.

**Results:**

Using this analysis, the ASD group had significantly more risk factors indicating low progesterone than controls (1.21 ± 0.09 vs. 0.76 ± 0.08, p< .0001),

**Conclusions:**

Our results support our hypothesis that low progesterone may be responsible for both obstetrical complications and brain changes associated with autism. Moreover, low progesterone could explain the male preponderance of autism (since only the developing male brain expresses progesterone receptors) and the increased incidence of autism could be explained by advances in fertility and obstetrical management masking progesterone deficiencies. We are currently expanding our studies to determine the role of low progesterone in specific components of the autism spectrum.

Our work suggests that progesterone levels should be routinely monitored in at-risk pregnancies.

**175.099 99** Maternal Metabolic Conditions and Neonatal Cytokine and Chemokine Levels of Children with ASD. P. Krakowiak*[1], I. Hertz-Picciotto[2] and J. Van de Water[2], (1)*University of California*, (2)*UC Davis*

Background: Previous studies have reported increased blood concentrations of pro-inflammatory cytokines and chemokines, such as Tumor Necrosis Factor (TNF)α, interleukin (IL)-6, IL-1β, Monocyte Chemotactic Protein (MCP)-1, Macrophage Inflammatory Protein (MIP)-1α, and Regulated upon Activation, Normal T-cell Expressed, and Secreted (RANTES), among individuals with metabolic conditions (MCs; obesity, diabetes, hypertension) compared with healthy controls. Moreover, higher IL-6 levels have been detected in the cord blood of newborns born to obese mothers compared to lean mothers. Animal model studies have linked maternal inflammation to microglial activation and stimulation of pro-inflammatory cytokine production within the fetal hippocampus resulting in increased neurocognitive effects in offspring that continued into adulthood. Several clinical and epidemiologic studies have also reported associations between metabolic conditions in pregnancy and adverse neurodevelopmental outcomes in offspring including autism spectrum disorder (ASD). Aberrations in the immune response of individuals with ASD compared with typically developing (TD) controls have been documented in numerous studies. These studies

led us to our hypothesis that some dysregulation in immune function of individuals with ASD may be attributed to prenatal exposure to maternal metabolic conditions.

Objectives: In this preliminary study, we examined whether neonatal cytokine and chemokine levels differed in ASD cases versus controls with and without prenatal exposure to maternal metabolic conditions.

Methods: A subset of 2 to 5 year-old participants from the CHARGE (*CH*ildhood *A*utism *R*isks from *G*enetics and the *E*nvironment) Study with (1) a confirmed diagnosis of ASD or TD, (2) cytokines and chemokines measured in newborn blood spots (archived as part of the California Newborn Screening Program), and (3) data on maternal metabolic conditions were included in the study. Median concentrations of analytes (IL-1β, IL-6, TNFα, IL-10 MCP-1, MIP-1α, and RANTES) were estimated using quantile regression models adjusted for child's age at blood spot collection, time between collection and sample elution, cesarean delivery, labor duration, and gestational age. Analyte concentrations were normalized to total protein content.

Results: Among ASD cases, children of mothers with MCs had significantly higher median IL-6 concentrations compared to children without exposure to maternal MCs ($P$=0.04). No differences in IL-6 levels were detected according to maternal MCs among controls. Conversely, among controls, lower median TNFα concentrations were observed in children of mothers with MCs ($P$=0.01). No differences in TNFα levels were found among ASD cases with respect to maternal MCs. MIP-1α concentrations were marginally higher in children with maternal MCs among controls ($P$=0.06). Among children exposed to maternal MCs, ASD cases had marginally lower MIP-1α levels than controls ($P$=0.06). No other differences in cytokines or chemokines were detected with respect to child's case status or maternal MCs.

Conclusions: These preliminary findings suggest that newborns later diagnosed with ASD appear to exhibit a different immune profile in association with maternal MCs compared with controls. Given the link between inflammation and metabolic conditions, prenatal exposure to maternal metabolic conditions may potentially contribute to immune dysregulation in offspring.

**175.100 100** Modulation of the Serotonin Transporter By Interaction with N-Ethylmaleimide-Sensitive Factor. K. Iwata*[1], H. Matsuzaki[2], T. Katayama[3] and N. Mori[4], (1)*Fukui Univ.*, (2)*University of Fukui*, (3)*Osaka University United Graduate School of Child Development*, (4)*Hamamatsu University School of Medicine*

Background: Many studies on the pathophysiologic mechanism of autism have focused on the serotonergic system. Prior studies consistently found elevated serotonin levels in the whole blood cells and platelets of patients with autism. Importantly, our colleagues reported that serotonin transporter (SERT) and its radioligand binding was significantly lower throughout the brain in autistic individuals compared with controls (Nakamura et al., 2010). These clinical evidences suggest that SERT function may be disturbed in autism. The functions of neurotransmitter transporters are influenced both by the number of transporter molecules present at the cell surface and by the intrinsic activity of individual transporter molecules. It is known that the number and activity are regulated by proteins which interact with transporter. Several SERT-interacting proteins, such as SCAMP2, nNOS, Hic-5 and syntaxin-1A, have been identified mainly by yeast two-hybrid screens. However, it is little known whether some of these proteins bind SERT in the mammalian brain.

Objectives: In this study, we sought to identify novel SERT-interacting proteins and investigate whether one of such protein regulates SERT function.

Methods: Novel SERT-binding proteins were examined by a pull-down system. Alterations of SERT function and membrane expression upon knockdown of the novel SERT-binding protein were studied in HEK293-hSERT cells. Endogenous interaction of SERT with the protein was evaluated in mouse brains.

Results: *N*-ethylmaleimide-sensitive factor (NSF) was identified as a novel SERT-binding protein. NSF co-localized with SERT at the plasma membrane, and NSF knockdown resulted in decreased SERT expression at the cell membranes and its uptake function. NSF endogenously co-localized with SERT and interacted with SERT.

Conclusions: It has been reported that NSF interacts with some neurotransmitter receptors, such as glutamate, adrenaline, and dopamine receptors, and regulate membrane trafficking of these receptors. Since it has been reported that many of these receptors are abnormal in autism, it is possible that NSF plays a key role in the pathophysiology of the disorder.

**175.101 101** Molecular Analysis of Inflamed Ileocolonic Tissue from GI Symptomatic ASD Children. S. J. Walker*[1] and A. Krigsman[2], (1)*Wake Forest University Health Sciences*, (2)*Pediatric Gastroenterology Resources of New York and Texas*

**Background:** Gastrointestinal symptoms are common in children with autism spectrum disorder (ASD) and are often associated with mucosal inflammatory infiltrates of the small and large intestine. Whole transcriptome analysis of biopsy tissue from ASD$^{IC}$ (ASD with ileocolitis) and non-ASD IBD (Crohn's disease and ulcerative colitis) patients has provided molecular evidence for an overlapping, yet unique, IBD-like condition in ASD children. Here we examine the genes and biological pathways that are differentially regulated between inflamed and non-inflamed ileocolonic tissue.

**Objectives:** The purpose of this study was to evaluate the molecular mechanisms that underlie inflammation in the large and small intestines of ASD$^{IC}$ children.

**Methods:** Study tissue consisted of ileocolonic biopsies from two groups of children undergoing ileocolonoscopy for active gastrointestinal symptoms: (1) those with an ASD diagnosis and, (2) typically developing children. All tissue specimens were collected under appropriate IRB approval. For each ASD individual two biopsies (one from terminal ileum, one from colon) that demonstrated the histologic presence of either ileal infiltrates (ileitis), colonic infiltrates (colitis) or both (ileocolitis) were used. Two histopathologically normal tissues from the identical locations were obtained from each control individual for comparison. Total RNA was isolated from the tissue biopsy specimens and used to query whole genome DNA microarrays. Pair-wise comparisons of gene expression were made between ASD$^{IC}$ and control groups for each of the two tissues. Lists of DEGs (differentially-expressed genes) in ASD$^{IC}$ terminal ileum and colon were then evaluated for overrepresentation in gene ontology categories and biological pathways.

**Results:** Pair-wise analyses between ileal mucosa from ASD$^{IC}$ and non-inflamed control samples resulted in 4017 DEGs, of which 66% were down-regulated in the ASD group. This gene set was significantly associated with cancer, inflammatory response and immunological disease. Overall, numerous important metabolic pathways were highly significantly down-regulated in the terminal ileum - they included protein digestion and absorption, pancreatic secretion, bile secretion, fatty acid metabolism, glutathione metabolism and carbohydrate digestion and absorption. In contrast, the majority (61%) of DEGs in colonic tissue were up-regulated. These genes, as a group, were highly associated with cancer and gastrointestinal disease. Many of the biological pathways significantly up-regulated in the colon, for example NOD-like receptor signaling and granulocyte adhesion and diapedesis, are involved in activation of immune response. Of the 4017 DEGs identified in the terminal ileum and 2796 identified in the colon samples, 972 DEGs were common between the two tissues. These shared DEGs were significantly associated with cancer, inflammatory response and, interestingly, neurological disease.

**Conclusions:** Taken as a whole, the picture that emerges is one in which GI symptomatic children with ASD in whom cellular infiltrate is present in the ileum and/or colon have a distinct molecular signature that is consistent with gastrointestinal disease and is associated with digestive system development and function and also with neurological disease.

**175.102 102** Oxidative Stress and Immune Cytokines in Plasma of Young Children with Autism Spectrum Disorder and Recent Language and/or Social Regression: A Prospective Case-Control Study. A. Loh*[1], E. Anagnostou[2], D. U. Menon[3], C. A. Pardo[4], J. A. Brian[5], T. Clemons[6], M. L. Bauman[7], A. W. Zimmerman[8], M. E. Fenwick[9] and S. J. James[10], (1)*Surrey Place*, (2)*Holland Bloorview Kids Rehabilitation Hospital*, (3)*Kennedy Krieger Institute*, (4)*Johns Hopkins University School of Medicine*, (5)*Holland Bloorview Kids Rehab/ Univerisity of Toronto*, (6)*The Emmes Corporation*, (7)*Boston University School of Medicine*, (8)*Lurie Center for Autism Massachusetts General Hospital*, (9)*University of Calgary*, (10)*University of Arkansas for Medical Sciences*

Background: Regression occurs in 22%-41% of children with Autism Spectrum Disorder (ASD) at

the average age of 20-23 months. At present, no clear contributors to regression have been identified. Increased levels of several immune cytokines have been reported in the subgroup of regressive autism, but no studies have examined the role of oxidative stress in this process.

Objectives: To compare biomarkers of oxidative stress and immune cytokines in children with ASD, with and without regression.

Methods: Three sites in the Autism Speaks Autism Treatment Network: Toronto, ON; Baltimore, MD; and Little Rock, AS, recruited children, aged 18-42 months with ASD, with regression (ASD-R) (n=25), and without regression (ASD-NR) (n=24). The two groups were compared with regards to oxidative stress markers (free reduced glutathione, oxidized glutathione, homocysteine, cysteine, 3-nitrotyrosine and 3-chlorotyrosine) and immune cytokines (interleukin 1, macrophage chemoattractant protein 1, macrophage inflammatory protein 1A, interferon gamma, TNF alpha, and CD 40L). Regression was defined as having established a skill for at least one month, followed by a significant loss of that skill (more than 90% for language, and 75% for social) for more than 1 month. Regression was operationalized using a modified Regression Validation Interview and inter rater reliability for the assessment of "definite" or "no" regression was 89%. The ASD-R group completed a standardized medical investigation including screening for metabolic and genetic disorders. Children met criteria for an ASD according to the Autism Diagnostic Observation Schedule and the DSM-IV.

Results: The mean ages of the ASD-R and ASD-NR groups were similar, 2.5 and 2.6 years respectively. The mean age of regression in the ASD-R group was 1.9 ± 0.4 years and the duration from when regression was definitively noted to plasma analysis was 8.0 ± 4.5 months. The ASD-R group had a significantly lower mean free reduced glutathione level (1.71 ± 0.13) compared to the ASD-NR group (1.86 ± 0.20) ($p=0.006$). There was also an increase in a marker for protein oxidative damage, 3-nitrotyrosine ($p=0.04$) in the ASD-R (74.19 ± 17.14) compared to the ASD-NR (64.78 ± 12.30) group. There were no differences in other oxidative stress markers or immune cytokines between groups.

Conclusions: In this pilot study, ASD and recent regression in young children was associated with decreased free glutathione and increased 3-nitrotyrosine, supporting evidence of decreased antioxidant potential and increased oxidative damage in plasma, compared to young children with ASD and no regression. There were no group differences in other biomarkers of oxidative stress. Lower free glutathione levels may be a risk factor for regression in a subgroup of children with ASD and regression. This study was limited by a small sample size and the analysis of oxidative stress biomarkers and cytokine levels was limited to plasma. Future studies should examine oxidative stress biomarkers in the plasma and cerebrospinal fluid in young children with ASD and recent regression to assess for possible differences in oxidative stress and damage in the central nervous system.

## 176 Specific Interventions - Non-Pharmacologic

**176.103 103** Effects of Cognitive-Behavioral Intervention on Emotion Regulation in Adults with High-Functioning Autism Spectrum Disorders: A Randomized Controlled Trial. M. Kuroda*[1], Y. Kawakubo[1], H. Kuwabara[2], Y. Kamio[3] and Y. Kano[4], (1)*University of Tokyo*, (2)*University of Tokyo Hospital*, (3)*National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*, (4)*The University of Tokyo*

Background: Adults with high-functioning autism spectrum disorders (ASD) have difficulties in social communication and therefore have deficits in understanding others' minds. Recent research has found that they are unable to understand not only others' but also their own minds. This could lead to difficulties in self-regulation. Some studies have reported the effectiveness of cognitive-behavioral therapy (CBT) in improving self-regulation for the children with ASD.

Objectives: This study investigated the efficacy of group-based CBT for adults with ASD.

Methods: The study was a randomized, waiting list controlled, open-blinded trial (This trial was registered in The University Hospital Medical Information Network Clinical Trials Registry No. UMIN000006236). Participants were planned to be 30 adults with ASD in CBT group and the waiting list control group. Primary outcome measures were the 20-item Toronto Alexithymia Scale (TAS20), the Coping Inventory for Stressful

Situations (CISS), the Motion Picture Mind-Reading (MPMR) task and a questionnaire about ASD. The secondary outcome measures were the CES-D, The QOL, the GAF scales, the State-trait Anxiety Inventory (STAI), the Social Phobia and Anxiety Inventory (SPAI) and the Liebowitz Social Anxiety Scale (LSAS). On the pre (within 4 weeks), post (within 4 weeks) and 12 week follow up period of the intervention, the all measures were examined. CBT group received group therapy over a 8-week period (1 session/week) with each session lasting approximately 100 min. Each group during therapy consisted of 4~5 adults with ASD and 2 psychologists. We used the visual materials for this intervention, mainly the Cognitive Affective Training (CAT) kit (Attwood, 2008).

Results: A total of 82 individuals with ASD were referred to this study. Of these, 60 (73.2 %) met inclusion criteria. For each of the outcome measures, we calculated the differences between pre- and post-assessment, pre- and follow-up assessment, and post- and follow-up assessment scores. Differences between the control group and the waiting group were assessed using t-tests. These t-tests demonstrated significant differences ($p < 0.05$) between pre- and post-assessment scores on the TAS Factor 2, the ASD questionnaire (attitude), and between pre- and follow-up assessment scores on the CISS (E). Additionally, there were marginally significant differences ($0.05 \leq p < 0.1$) between pre and post-assessment scores on the CISS (T), GAF, and LSAS (A); between post- and follow-up assessment scores on the SPAI-(S) and CES-D; and between pre- and follow-up assessment scores on the GAF and LSAS (E & A).

Conclusions: Our group-based CBT for adults with ASD improved their understanding of their own emotions and thoughts, increased their positive thinking regarding ASD, and enhanced their coping skills. There was some improvement in secondary symptoms, such as anxiety, depression, and social function. Therefore, this group-based CBT was effective. A limitation of this study was that the improvement regarding their understanding of their own emotions and thoughts, and their positive thinking towards ASD, could not be sustained. It was not clear whether such improvements were caused solely by the program's curriculum, or by the additional effects of the group. Further studies should implement this program in the form of one-on-one sessions.

**176.104 104** A Computer-Assisted Social Intervention for College Students with ASD: Assessment of Longitudinal Changes in White Matter Integrity in a Small, Randomized Controlled Trial.

J. A. Richey*[1], S. W. White[2], D. Gracanin[1], M. Coffman[1], M. Ghane[3], K. Gad[1] and S. Laconte[1], (1)*Virginia Tech*, (2)*Virginia Polytechnic Institute and State University*, (3)*San Diego State University*

Background:

The number of college students with Autism Spectrum Disorders (ASD) enrolled in public and private higher education institutions has been growing steadily over the last several years (White, Ollendick & Bray, 2011). These young adults face considerable interpersonal and daily living obstacles, despite intact cognitive abilities, yet there are no empirically supported interventions to support social and academic function in young adults with ASD. In the current study, we evaluated the feasibility and preliminary efficacy of a new, computer-based protocol for college students with ASD, along with neuroimaging data before and after treatment. In a pilot randomized controlled trial (n = 8), we evaluated a 12- week, novel virtual-reality brain-computer interface (VRBCI) intervention against a psychosocial intervention of the same duration: College and Living Success (CLS). All participants (5 males, 3 females) were college undergraduates, free of intellectual disability, and confirmed to have ASD via ADOS. At baseline, we conducted several neuroimaging protocols including anatomical (T1-weighted), resting-state fMRI and diffusion tensor imaging (DTI). We hypothesize that at post-treatment the VRBCI group will demonstrate changes in superior longitudinal fasciculus and uncinate fasciculus as compared to CLS. This hypothesis is based on a recent meta-analysis of 25 DTI studies in autism (Aoki et al., 2013) that highlight potential roles for these regions of interest. This prediction is also based on emergent evidence that these major white-matter tracts may play a role in communicative abilities (Nagae et al., 2012; Pardini et al., 2012), which are a target in our VRBCI intervention.

Objectives:

Evaluate preliminary neuroimaging results for evidence of structural (MRI, DTI) and functional

(rs-fMRI) reorganization as a function of intervention condition.

Methods:

We computed global probabilistic tractography using anatomical priors in FSL and Freesurfer (BEDPOSTX and TRACULA, respectively). Bayesian estimation of diffusion priors and subsequent estimates of connectivity distributions in FSL were used to estimate first level diffusion parameters, which were then passed to the second level for random effects analysis.

Results:

At baseline, preliminary results indicate no difference between the groups in fractional anisotropy (FA) values, suggesting at a minimum that random assignment was effective. At post treatment (December, 2013), we will collect follow-up data on all subjects and evaluate potential differences in structural and functional reorganization of the longitudinal fasciculus and uncinate fasciculus between treatment conditions.

Conclusions:

Although our data come from a small pilot trial and statistical power is known to be limited as a result, we expect that some measurable differences will be observed as a function of random assignment, providing preliminary evidence for treatment effects at the neural systems level.

**176.105 105** A Targeted Intervention for Siblings of Children with Autism Spectrum Disorders: The Effects of a Sibling Support Group. A. P. Cohen*[1] and S. L. Harris[2], (1)*Medical University of South Carolina*, (2)*Rutgers University*

Background: The sibling relationship provides a unique context for the development of interpersonal skills and lays the groundwork for extensive social situations with other children. Siblings of children with autism spectrum disorders (ASDs) experience multiple stressors and increased caregiver demands that children with neurotypical siblings do not face. While some siblings do not experience significant adjustment problems, it appears that other children may have greater vulnerability to the development of significant adjustment problems and internalizing disorders. Very few studies have investigated the effect of a support group for children who have a sibling with ASD.

Objectives: The present study evaluated the effects of Project SibSTAR (Straight Talk about Autism Realities), an eight week support group that incorporated didactics, discussion, and role plays while using rigorous research design and psychometrically-sound measures.

Methods: Twenty siblings of children with ASD, ages 8-11, were randomized to either the active or delayed intervention group. While the groups received the same intervention, the time-lagged design allowed for the assessment of a multiple baseline design across both groups and skills. In addition, participants reported on measures of psychological and social functioning at baseline, post group, and 6 week follow-up assessments. Outcomes were assessed across a variety of domains, including intervention acceptability, concepts taught during group, play-based behavioral principles, and self-report of internalizing symptoms, self-competence, and perceived social support.

Results: Results indicated that participants increased their knowledge of autism, coping and problem solving skills, and their knowledge of behavioral skills. Further, trend level decreases in internalizing symptoms were found from baseline to post group assessment, and significant differences were found on measures of perceived social support and social self-competence. Meausures of social validity and treatment adherence and feasability indicated that treatments were well-received by participants and parents, targeted important goals, and were reliably applied using a manualized framework.

Conclusions: Siblings of children with ASD are an often overlooked group who present with unique stressors. This pilot for a manualized sibling support groups demonstrated positive psychosocial effects as well as increased knowledge about ASD. The authors advocate that support for siblings should move towards an evidence-based model which is readily available to community practitioners.

**176.106 106** Adaptation and Preparation for Conducting a Parent-Implemented Autism Intervention Among Underserved Families in Taiwan. P. F. Chen*[1], A. C. Stahmer[2], S. R. Reed[2], P. C. Tsai[3], Y. T. Wu[3], C. C. Wu[4], F. W. Lung[5] and L. C. Lee[3], (1)*Calo Psychiatric Center*, (2)*University of California San Diego*, (3)*Johns Hopkins Bloomberg School of Public Health*, (4)*Department of Psychology, Kaohsiung Medical University*, (5)*Taipei City Hospital*

**Background**: Research consistently demonstrates that access to early intervention is associated with positive cognitive, adaptive, behavior, and language outcomes for children with autism spectrum disorder (ASD). Due to a lack of existing infrastructure and the absence of resources to deliver clinic- or school-based interventions for ASD in some regions of Taiwan, there is a need to provide feasible, low-cost intervention to families who have a child with ASD. Parent-mediated intervention and behavioral management are particularly suitable for these families to implement at home. Pivotal Response Training (PRT) is an evidence-based, naturalistic, behavioral intervention with a clear structure that can be used to target a variety of goals. These characteristics make PRT a good fit for the target population in Taiwan. Because local culture treats adults (i.e., parents or grandparents) as authoritative figures, more relationship-focused interventions may not be as accepted. However, cultural adaptation is likely needed to ensure PRT is appropriate for this group and acceptable to families.

**Objectives**: To describe 1) cultural and social characteristics of socioeconomically disadvantaged families in Taiwan affected with ASD, and 2) challenges and barriers in adaptation, preparation and implementation of a parent-mediated ASD intervention for these families.

**Methods**: To prepare for full study implementation, a pilot study was conducted to test cultural sensitivity, appropriateness, and relevance of the instruments and questionnaires. Qualitative information was obtained through interviews with primary caregivers and local professionals who work with families affected by ASD. These interviews were conducted to gain knowledge about family needs and priorities for intervention in underserved families.

**Results**: Characteristics of study families include: very low SES, grandparents as primary caregivers, single-parent households, and dialects speaking households. Although national universal health care coverage is available in Taiwan, underserved families with a child with ASD report either never seeing a health care professional for developmental or behavioral issues or having significantly delayed diagnosis determination. Pilot results indicate that lack of autism awareness, barriers to accessing care (e.g., low literacy levels, limited knowledge about the health care system, no transportation), and lack of understanding the need to intervene in ASD are common reasons for not accessing intervention. In addition, results indicate cultural differences (e.g., limited use of praise, different behavioral goals, limited toy access) might require intervention adaptation. Instead of a typical PRT program, a culturally modified version with emphasis on behavioral management may address concerns that are most-pressing to caregivers and therefore improve the likelihood of parent-implementation.

**Conclusions**: Some barriers to accessing autism interventions are similar to what is observed in Western populations, while others are unique to this culture. The magnitude of such challenges is overwhelming for these families. It is our hope that, by training parents as therapists in culturally appropriate ways, barriers to access will be overcome. Upon completing the project, the adapted program will be available for implementation nationwide to communities or families with few resources in Taiwan. The full study is ongoing and completion is expected by February 2014. Preliminary findings and specific cultural adaptations will be discussed.

**176.107 107** An Autism Spectrum Disorder (ASD) Clinical Trial: Rater Training Program Overview and Initial Findings. L. Kingery*[1], P. Ventola[2], X. Liogier D'ardhuy[3], M. Deraët[3], A. E. Veroff[1], S. Zaragoza[1], V. Krishna[1], A. P. Nomikos[1], A. Miner[1], M. del Valle Rubido[3] and O. Khwaja[4], (1)*Cogstate*, (2)*Yale University*, (3)*Roche*, (4)*F.Hoffmann-La Roche AG*

Background: Ensuring reliable and valid screening and outcome assessments in Autism Spectrum Disorders (ASD) trials is challenging; ASD is a behaviorally-defined disorder, measures are complex and diverse, including cognitive/neuropsychological tests, clinical global impression ratings, caregiver interviews, and caregiver- and patient-reported outcomes (PROs). A further challenge is many of these assessments require unique rater skills. For this phase II clinical trial involving 26 US sites, the customized rater training/assessment program included rater prequalification, five rater roles, didactic training for all scales, including expert consultants, required practice, and rater certification procedures assessing rater competency. Raters also completed a post-Investigators' Meeting (IM) training experience survey.

Objectives: Summarize key considerations for rater training programs in ASD, present information about site/rater experience in an ASD clinical trial, summarize relationships between pre-qualified rater experience and rater performance on certification assessments.

Methods: All potential raters completed a Rater Experience Survey (RES) of education, clinical experience with ASD, and scale-specific experience. Rater certification data included scores on mock scoring exercises, quizzes, and practice administrations. Relationships among these variables were examined using analysis of variance and correlation techniques. A rater survey post-IM gathered structured and open-ended responses, which were summarized descriptively and qualitatively.

Results: Thus far, 125 potential raters completed a RES, of which 118 met pre-qualification criteria and entered the rater training/certification program. Pre-qualified raters' educational background varied: 13 raters with bachelor degrees, 34 with master degrees, 29 with doctoral degrees (PhD, PsyD), 42 with medical degrees (MD). ASD clinical experience varied, ranging from 0 to 40 years (mean =9.56, SD=7.90). Scale-specific experience was also evaluated and varied from no experience to extensive experience, depending on the scale. Most raters performed well on training vignettes for a clinician-rated scale (Ohio Autism Clinical Impression Scale; OACIS) and a quiz on administration practices for the Vineland Adaptive Behavior Scale-II; VABS-II). Rater performance on certification materials for neuropsychological tests (Wechsler Abbreviated Scale of Intelligence; WASI-II, Repeatable Battery for the Assessment of Neuropsychological Status; RBANS) varied from no errors to many. Results of the rater survey after the IM indicated differences in the value raters see in hands-on training. Less experienced raters stated need for more individual time with the trainers; more experienced raters requested abbreviated training requirements. However, in the hands-on training, several experienced raters made unexpected errors, validating the need for their participation. Preliminary analyses examining the relationship between ASD clinical experience, education, and performance on the training/certification materials for pre-qualified raters suggest no significant relationship among these variables. For one test, the WASI-II, previous experience with the scale was associated with fewer scoring errors on the rater assessment materials. In addition, we also observed that a small number of raters were responsible for a disproportionate number of total rater errors across all raters.

Conclusions: Even clinical trial raters who meet pre-qualification criteria are highly diverse in their clinical and scale-specific experience, and not always aware of the errors they make despite their experience. Comprehensive training and individual assessment are required to prepare raters for testing clinical trial study subjects.

**176.109 109** Assessment of Intervention Effects on in Vivo Peer Interactions in Adolescents with Autism Spectrum Disorders.
B. K. Dolan*, A. V. Van Hecke, B. Gemkow, J. Kahne, N. Linneman and R. J. Remmel, *Marquette University*

*Background:* Social skills deficits among individuals with ASD lead to isolation and lack of friendships. The Program for the Education and Enrichment of Relational Skills (PEERS: Laugeson, Frankel, Mogil, & Dillon, 2009) is an empirically based, manualized, outpatient treatment program designed to teach motivated adolescents with developmental delays the social skills needed in order to make and keep friends (Laugeson et al., 2009). To date, there are no known published studies that have assessed the effectiveness of social skills intervention for adolescents with Asperger's Syndrome (AS) or high functioning autism (HFA) via an observational method. Specifically, previous studies have relied on self-report measures from parents, adolescents, or teachers about the improvement of social skills.

*Objectives:* The study sought to evaluate the effectiveness of a randomized controlled trial of a social skills intervention program, the Program for the Education and Enrichment of Relational Skills (PEERS), by coding a digitally recorded, *in vivo*, social interaction between adolescent participants with ASD and a typically developing adolescent.

*Methods:* The analysis included 45 adolescents (11 to 16 years-old) with ASD. All participants had a verbal IQ > 70 and diagnoses were confirmed with the ADOS. The intervention was the 14-session Program for the Enrichment and Education of Relational Skills (PEERS: Laugeson et al., 2009). Measures were taken at pre-intervention and post-intervention and included: (1) a 10-minute videotaped social interaction with

an unfamiliar, typically developing, gender-matched adolescent, and (2) the *Test of Adolescent Social Skills*(self-report; TASSK; Laugeson & Frankel, 2006). Adolescents' social interactions were later coded using the Contextual Assessment of Social Skills (CASS: Ratto, Turner-Brown, Rupp, Mesibov, & Penn, 2010).

*Results:* For the experimental group, adolescents' *in vivo* social skills increased from pre- to post-treatment, but these changes did not reach traditional levels of significance. Social skills knowledge, as assessed by the TASSK, demonstrated significant differences between the experimental and waitlist control groups, with the experimental group indicating greater improvements in social skill knowledge at post-treatment (Wilks' Lambda = 1.57, $F(1, 43) = 230.51$, $p < .05$). Planned analyses will include two additional cohorts to further assess the effects of the interaction on the *in vivo*interactions.

*Conclusions:* Adolescents receiving the PEERS intervention demonstrated increases in social skill knowledge, and their peer interactions suggested trends toward increases in *in vivo* social skills. The results of this study added to the minimal literature regarding social skills development in this population, and highlight the importance of observational data.

**176.110 110** Autism and Safety- It's Unpredictable. J. Harris* and A. P. Robertiello, *Children's Specialized Hospital*

**Background:**
Safety is a major concern among people with autism spectrum disorder (ASD). Statistics show that 49% of children with ASD wander or elope from safe settings. Indeed, cases involving missing children with this disorder are reported in the media frequently. Unfortunately, the outcome often is all too tragic. Reports indicate that 32% of parents of children with ASD have indicated a "close call" with a possible drowning. In addition, children with ASD are particularly vulnerable during emergency situations which include weather-related events, fires, and power outages. There may also be special challenges for police and criminal justice staff when people with ASD are victims, witnesses or perpetrators involved in criminal matters. The reasons for increased vulnerability include communication, social, behavioral and cognitive challenges; sensory factors; and limited recognition and understanding of these challenges by family, community members and safety personnel. While widespread, data on injury involving people with ASD is under-reported in part because victims may not be identified as having a disability.

**Objectives:**
To provide education and resources which focus on safety matters and emergency preparedness related to people with ASD and those who protect them. The goals are to increase understanding and recognition of people with this disorder; improve effectiveness of interactions and adaptive response techniques; improve the effectiveness of emergency response; and to reduce the number of emergencies involving people with ASD and/or lessen severity of potential events. Increased awareness may also impact accuracy of reported statistics regarding injuries or fatalities involving people with ASD.

**Methods:**
A comprehensive training program, *Autism and Safety: It's Unpredictable* will be described. This program has been implemented with families, service providers in the general community including first responders, fire prevention officials, emergency response and disaster staff, police, prosecutors and other court officials, juvenile detention personnel, school staff, and afterschool service providers. Supportive materials were developed and will be reviewed including family and community safety guidebooks, tools to educate people with ASD about 911, tools for 911 emergency dispatchers regarding identification and communication with people who have ASD, safety profile sheets and identification systems, and anti-bullying strategies. The developed materials include print and web-based tools, videos and articles.

**Results:**
Over 800 people have received safety-related training. Findings will be reviewed regarding reported changes in level of awareness, understanding, and confidence in interacting with people with ASD among community service providers. Family responses will be reviewed including prevention strategies implemented and changes noted in safety-related knowledge.

**Conclusions:**
Safety is a critical issue among people with ASD. Community service providers and families have been very receptive to this education. This

training has led to changes in practices which are expected to result in increased recognition of autism-related interactions; assessments of more accurate data capture of safety incidents; expanded strategies and resources for emergency management; as well as safer environments for people affected by this disorder.

**176.111 111** Clinical and Biomarker Effects of a Novel Vasopressin 1a Receptor Antagonist Vs Placebo in High Functioning Adult Autism. E. Hollander*[1], M. del Valle Rubido[2], O. Khwaja[3], L. Squassante[4], C. J. Ferretti[5], B. P. Taylor[6], G. Berlin[7], R. H. Noone[5], L. Antar[5], J. T. McCracken[8], L. Scahill[9], F. Shic[10], R. J. Jou[11], M. C. Lyons[11], A. Gavaletz[11], C. A. Wall[10] and D. Umbricht[12], (1)*Montefiore Medical Center University Hospital, Albert Einstein College of Medicine*, (2)*Roche*, (3)*F. Hoffman-La Roche Ltd.*, (4)*F-Hoffmann-La Roche Ltd.*, (5)*Montefiore Medical Center, Albert Einstein College of Medicine*, (6)*Montefiore Medical Center/Albert Einstein College of Medicine*, (7)*Albert Einstein College of Medicine*, (8)*UCLA Semel Institute for Neuroscience & Human Behavior*, (9)*Marcus Institute, Emory University*, (10)*Yale University School of Medicine*, (11)*Yale University*, (12)*F. Hoffmann - La Roche AG*

Background:

Oxytocin and vasopressin play a critical role in social cognition and social signalling deficits of ASD. Experimental therapeutic interventions to enhance oxytocin or block Va1A receptor signalling may modulate these domains in ASD

Objectives:

To explore the impact of a novel V1a antagonist R050288442 vs placebo on core social cognition measures, exploratory biomarkers, and safety/tolerability measures in adult high functioning ASD.

Methods:

High-functioning adults (M=23.4 years, range=18 to 40 years) with autism (*n*=19) participated in a multi-center (3-site), randomized, double-blind, placebo-controlled, cross-over study of the effects of novel vasopressin 1a receptor antagonist R050288442 . Each participant was seen on two separate days (1 week apart) for dosing a 2 hour infusion of R050288442 or placebo. Safety/tolerability, PK, PD, core social cognition, olfaction, language sampling and AVPR1A polymorphisms measures were collected.

Results:

At baseline, the Affective Speech Recognition (ASR), Reading the Mind in the Eyes (RMET) and olfaction measures correlated with measures of functioning on the Vineland and ADOS as well as IQ. The Va1 antagonist showed evidence of anxiolysis. The Va1 antagonist showed effects on olfaction, RMET and scripted interaction in the predicted direction of modest effect sizes. There were large negative effect sizes of the Va1a antagonist vs placebo on the social cognition ASR measure Lust and Fearful subscales, and there appeared to be carryover effects from infusion 1 to infusion 2 that may influence these findings.

Conclusions:

This study provides preliminary evidence of the ability of a novel V1a antagonist R050288442 to affect core symptoms of social cognition and olfaction. Effects on the laying down of social memory and social learning may persist well past the pharmacokinetic effects of the compound. These results should be taken as preliminary but may help to guide the development of new oral vasopressin antagonist interventions in ASD.

**176.112 112** Group Autism Parent-Training in a Low-Resource Community: A Randomized Controlled Trial of a Joint Engagement Intervention in Buenos Aires, Argentina. K. Houghton*[1], A. Rattazzi[2], S. H. Cukier[2], P. Landolfi[2], N. Martinez[2] and C. Lewis[1], (1)*Lancaster University*, (2)*PANAACEA*

**Background:** Parent-implemented interventions for young children with ASD have been found to be associated with improvements in child social engagement (e.g. Casenhiser and Shanker. 2011; Kasari et al.2010; Patterson, Elder, Gulsrud and Kasari, 2013) language (Coolican et al. 2010; Vismara et al. 2009), imitation (Ingersoll and Gergans, 2007), and play (Gillett and LeBlanc 2007). In countries with relatively few trained autism professionals, such as Argentina, parent-implemented interventions may be the only services available for young children with ASD. However, traditional parent training models emphasizing individual coaching sessions are not scalable in countries such as Argentina and very little research has focused on group parent training which has the potential to make training more accessible to families (Minjarez, Williams, Mercier and Hardan, 2011; Ingersoll and Dvortcsak, 2007). This study is the first randomized controlled trial of a group-parent training program for ASD in Argentina.

**Objectives:** The study aimed to test the efficacy of the parent-training program translated into Spanish and delivered in a 2-day weekend workshop format.

**Methods:** The parent-training program was originally developed for a multi-cultural, low-income, group in the Bronx, NY (Houghton and Lewis, 2012) and teaches parents research-based techniques for encouraging joint engagement embedded in everyday activities at home. 24 families, with children under 6 years of age with ASD, were randomly allocated to two groups. The primary dependent variable was parent interactive style, specifically Responsivity and Directiveness (Mahoney & Perales, 2003), as observed in a video recorded free play session with the child. Group 1 received the 2-day parent-training program first while Group 2 served as a control group. Then Group 2 received the training program, forming a secondary, multiple-baseline arm.

**Results:** Group 1 showed a significant increase in Responsivity and a significant decrease in Directiveness after the training program as compared to the control group. Group 2 showed the same pattern of change in interactive style as compared to the baseline period.

**Conclusions:** A brief, low-cost group parent-training program was shown to increase parent Responsivity and reduce Directiveness, an interactive style that has been shown to positively impact social-communication development in children with ASD.

**176.113 113** Can a Brief Behavioral Intervention Improve Sleep Hygiene in Adolescents and Young Adults with Autism Spectrum Disorders?. W. A. Loring*, L. L. MacDonald, L. Gray, R. L. Johnston, S. E. Goldman and B. A. Malow, *Vanderbilt University Medical Center*

Background: Sleep problems affect many individuals with autism spectrum disorders (ASD). Many studies of sleep problems in ASD have focused on young children, with less understood about the treatment of sleep problems in adolescents/young adults with ASD. Treatment of sleep problems with medications is not always successful and often has adverse effects. Behavioral treatment of sleep concerns for adolescents/young adults with ASD is an understudied area with many potential benefits. In this study, we employ an education-based program and are assessing the impact of the program on nighttime sleep and daytime functioning for adolescents/young adults ages 11-21 with ASD.

Objectives: Objectives of this study are to: 1) develop a manualized education program for adolescents/young adults with ASD and their parents and 2) assess the impact of this program on nighttime sleep and daytime functioning for adolescents/young adults with ASD.

Methods: The program consists of 2 individual education sessions with a psychologist, the adolescent/young adult, and their parent, followed by 2 follow-up phone calls. These sessions focus on components of successful sleep previously researched with children with ASD ages 2-10. This includes daytime habits, bedtime routines, sleep timing, and sleep environment. This program also includes the addition of strategies related to relaxation, distraction, and mindfulness-based breathing for the adolescent/young adult to utilize at sleep onset and during night wakings. The adolescent/young adult participant wears an actigraphy device to provide objective data concerning their pre- and post-program sleep. The parent and adolescent/young adult also complete pre- and post-program self-report measures to assess various aspects of sleep and daytime behavior.

Preliminary results from our first six completers of this program are presented here, focused on the three measures. One is the Adolescent Sleep Hygiene Scale (ASHS), focusing specifically on its cognitive subscale, as challenges were exhibited in this area for the majority of participants at baseline. Subscale examples include "I use my bed for things other than sleep," "I check my clock several times during the night," and "I go to bed and think about things I need to do." Another is a parent absorption interview administered during follow-up phone calls to assess parental understanding, implementation, and comfort level of concepts covered in the sessions. The final measure is an evaluation form parents complete at the end of the program regarding their satisfaction with the sessions.

Results: In our parent report of the ASHS cognitive subscale, 5 out of 6 of the participants reported improvement in the majority of the items. In our adolescent/young adult report of this

subscale, 4 out of 6 of the participants reported improvement in the majority or all of the items. For all participants, Parent Absorption Interview scores were 3-5 on a 5-point scale for all questions (higher numbers indicating more understanding, implementation, and comfort) and evaluation scores were 3-4 on a 4-point scale for all questions (higher numbers indicating more satisfaction).

Conclusions: The behavioral sleep education program shows promising results in improving sleep hygiene for adolescents/young adults with ASD, with high levels of parent implementation and satisfaction.

**176.114 114** Changing College Students' Conceptions of Autism: A Mixed-Methods Analysis. K. Gillespie-Lynch*[1], R. Obeid[2], C. M. Shane-Simpson[3], M. Dupiton[4], T. Cintula[5], C. Olender[4], D. Bublitz[2] and P. J. Brooks[2], (1)*Graduate Center - CUNY*, (2)*The Graduate Center - CUNY*, (3)*The Graduate Center at the City University of New York*, (4)*College of Staten Island*, (5)*College of Staten Island - CUNY*

**Background:**

College students with ASD may face lack of understanding from their campus communities. While a recent closed-ended survey of campus knowledge of ASD revealed more correct than incorrect responses, participants often indicated that there is only one effective intervention for autism, that autism is caused by vaccines, and that people with autism can't live independently (Tipton & Blacher, 2013). Although closed-ended surveys allow comparison across studies, they may scaffold appropriate responses. Qualitative coding of definitions of autism provided by middle-school children revealed largely accurate but sparse responses that often lacked reference to the core symptoms of autism, particularly restricted interests and repetitive behaviors (Campbell et al., 2011). Semi-structured interviews revealed that adults often view people with ASD as learning disabled and incapable of living independently (Huws & Jones, 2010). Using a mixed-methods approach, we examined knowledge of autism among college students, as well as potential benefits of an online training about autism.

**Objectives:**

1) Examine open-ended definitions of autism by college students.

2) Evaluate effects of an online training on conceptions of autism.

**Methods:**

Participants were recruited for an online training about ASD primarily from a psychology subject pool. Participants (*N*= 171) completed a pre-test (consisting of open-ended and multiple choice questions), the training, and a post-test. Open-ended responses were coded into non-mutually exclusive categories by independent coders after they achieved reliability (greater than 80% agreement on at least 20% of the sample). Not all coding categories are reported.

**Results:**

*Baseline Knowledge of ASD:*

*What is ASD?* 110 responses were coded "communication issues", 105 "social issues", 77 "disorder", 57 "restricted/repetitive interests", 51 "childish", 38 "diversity", 38 "cognitive issues", 28 "brain issues" and 21 "sensory issues."

*What are two challenges adults with autism face?* 99 responses were coded "social", 87 "independence", 34 "communication", 21 "discrimination", 19 "other/don't know", and 15 "cognitive".

*What does the future hold for people with ASD?* 47 responses were coded "other/don't know", 35 "treatments", 27 "opportunities", 19 "cure", 4 "employment", and 1 "college".

*Changing Conceptions of ASD:*

*What does the future hold for people with ASD?* After the training, responses coded "college" (35) and "employment" (43) increased.

*What are three techniques for teaching people with ASD?* Before the training, 48 responses were coded "visual", 41 "structured", and 21 "individualized" After the training, 92 responses were coded "visual", 57 "individualized", and 55 "structured."

Closed-ended responses suggest that the training increased understanding of DSM-5 criteria, gender and ethnic differences in diagnosis, links between giftedness and autistic traits in the general population, interest in friendship among people

with ASD, and variability in desire for a cure for autism (*p*s < .001).

**Conclusions:**

These results suggest that college students have greater understanding of the core difficulties associated with autism than middle-school students. However, both populations conflate autism with cognitive delays and are more aware of social symptoms than restricted/repetitive interests. The online training altered conceptions of autism. As Tipton and Blacher noted (2013), more widespread knowledge about diversity in ASD may facilitate the transition into college for students with ASD.

**176.115 115** Child Behavior Problems Moderate the Relationship Between Maternal Self-Regulation and Maternal Stress. C. M. Conner* and S. W. White, *Virginia Polytechnic Institute and State University*

Background:

Previous research has shown that parents, especially mothers, of a child with Autism Spectrum Disorder (ASD) experience more stress than mothers of typically developing children and children with other disabilities (Hayes & Watson, 2013). Interventions targeting parents with concepts such as mindfulness training found lowered stress among parents and lowered child difficulties indirectly (Beer, Ward, & Moar, 2013; Singh et al., 2006, 2007). However, while research has studied parental psychopathology's effect on child outcomes (Suveg, Jacob, & Payne, 2010), little has observed how child behavior problems (BP) interacts with maternal self-regulation (SR) and stress.

Objectives:

Given increased stress among mothers of children with ASD, it is important to understand the relationship between child BP and maternal SR on stress. The purpose of the current study was to explore whether child (BP) functioned as a moderator of maternal SR and maternal stress.

Methods:

Sixty-six mothers of children with ASD aged 4-17 participated in an online survey on mindfulness and stress. Mothers completed a demographics questionnaire, the Aberrant Behavior Checklist-Irritability (ABC-I; Aman, Singh, Stewart, & Field, 1985) to measure child BP, Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983) to measure global stress, Mindful Attention Awareness Scale (MAAS; Brown & Ryan, 2003), Emotion Regulation Questionnaire (Gross & John, 2003) to measure reappraisal, and the Adult Temperament Scale-Effortful Control (ATQ-EC; Rothbart, Ahadi, & Evans, 2000). The MAAS, ERQ- reappraisal, and ATQ-EC were summed to create a SR composite. Hierarchical multiple linear regression of the ABC-I and maternal SR composite, both mean-centered, on stress was conducted with an interaction term to observe whether child BP functioned as a moderator.

Results:

Maternal SR [block 1] was associated with lower stress ($R^2$= .293; $\beta$= -.128*; F* (1, 64) = 26.488, *p* < .000). Increased child BP [block 2] was also associated with increased stress ($R^2$= .063; $\beta$= .154*; F* (1, 63) = 6.152, *p* = .016). The interaction of maternal SR and child BP [block 3] significantly predicted increased stress ($R^2$= .042; $\beta$= .006*; F* (1, 62) = 4.292, *p* =.042). The interaction was examined by comparing the interaction at the mean, +1 standard deviation above, and -1 standard deviation below the mean of child BP. Simple slope tests indicated that the interaction was significant for all levels (low: $\beta$= .006; *p*= .042; mean: $\beta$= .006; *p*= .042; high: $\beta$= .006; *p*= .042). However, there was no significant main effect of SR on stress for mothers of children with high BP (low: $\beta$= -.192; *p*< .000; mean: $\beta$= -.128; *p*< .000; high: $\beta$= -.065; *p*= .137).

Conclusions:

Results indicate that severity of child BP moderates the effect of maternal SR on stress. For mothers of children with ASD with higher BP, maternal SR does not have a significant effect on perceived stress, while mothers of children with lower BP and higher SR abilities report lower stress than mothers with low SR. Implications include parent-targeted interventions, as parent-targeted interventions alone may not be as effective in alleviating stress for parents of children with severe BP.

**176.116 116** Effect of Trampoline Training on Motor Proficiency and Body Mass Index in Children with Autism Spectrum Disorders. C. Lourenço*[1], D. Esteves[2], R. Corredeira[3], A. Seabra[3] and P. Pinheiro[1], (1)*University of Beira Interior*,

(2)*Beira interior University*, (3)*Faculty of Sport, University of Porto*

Background: It is generally agreed that regular physical exercise promotes several benefits in people with Autism Spectrum Disorders (ASD) (SOWA, 2012). Children with autism spectrum disorders present significant and widespread changes in motor performance (Fournier, 2010) and hence a weaker motor performance (Pan, 2009), problems in maintaining balance and in motion planning (Vernazza-Martin *et al*. 2005). The use of trampolines potentially improves balance and motor proficiency of children with learning disabilities (Giagazoglou, 2013).

Objectives: This study aims to evaluate the efficacy of a twenty-weeks trampoline training (TT) program on motor proficiency and body mass index (BMI) for children with ASD.

Methods: Seventeen children (5 girls and 12 boys, age 4-10) were assigned to either a supplemental trampoline training (TG) or control group (CG). Both groups continued to participate in their regular education curriculum.

The groups were evaluated in the beginning (baseline), after 10 weeks and in the end of program (after 20 weeks). BMI was evaluated by height and weight measurement and motor proficiency used the Bruininks–Oseretsky Test of Motor Proficiency (2nd ed.), (BOT). Group results were compared using multivariate analysis of variance (ANOVA).

Results: The TT program resulted in significant increases motor proficiency (p=.000): TG children evolved from a total BOT score of 21.33±17.682 (baseline) to 35.17±17.747 after 20 weeks, while control group evolved from a total BOT score of 28.27±10.001 to 30.27±7.55. No statistical differences were found on BMI.

Conclusions: Trampoline training is an effective option to develop motor proficiency for children with ASD.

**176.117 117** Effects of Rhythm and Robotic Interventions on the Affective States of Children with Autism Spectrum Disorders. A. N. Bhat*, D. Gilewska, I. Park, S. Srinivasan, T. Gifford and L. P. Neelly, *University of Connecticut*

Background: Children with ASDs also demonstrate several behavioral and affective impairments that may indirectly influence their social interactions with others. For example, children with ASDs have a significant incidence of neutral or negative affect, behavioral problems, as well as difficulty with social connections and empathetic behaviors to others (Mazefsky et al., 2012). We are currently conducting two randomized controlled trials to evaluate the effects of two novel, movement-based interventions on the affective states of children with ASDs. Children with ASDs find musical activities enjoyable and motivating (Srinivasan & Bhat, 2013). Similarly, there is some anecdotal evidence for the use of robot-based interventions to promote social interaction skills in children with autism (Kozima et al., 2007).

Objectives: In the current project we compared the effects of robotic and rhythm interventions on the affective states of children with ASDs, specifically, positive, interested, neutral, and negative affect.

Methods: 36 children diagnosed with ASDs will be matched on age and level of functioning and randomly assigned to three training groups - a rhythm group or a robot group or a control academic group. Children received training sessions across a total of 8 weeks (2 sessions per week from experts and 2 more sessions from caregivers). The rhythm group engaged in music-based activities involving singing, joint rhythmic action, and whole-body coordination with an expert trainer and an adult model. The robot group engaged in imitation games involving whole body movements, drumming, and walking with a humanoid robot, Nao and an adult model. The academic group engaged in stationary, fine motor and academic activities including reading, building, and arts and crafts. We are coding for affective changes in all three groups across the early, mid, and late training sessions. Specifically, we code for positive, interested, negative, and neutral affect during the entire session.

Results: We have preliminary data from two low-functioning children with autism, one from the rhythm group and one from the robot group. Both children demonstrated an increase in positive and interested affect across weeks of training. The child in the rhythm group showed a 33% increase with more time spent in positive and interested affect with training. Similarly, the child in the robot group demonstrated a 23% increase with time spent in more positive and interested affect

with training. We hypothesize that overall, children in the rhythm and robot groups will enjoy the training activities more than the children in the academic group. We are continuing to code the remainder of the dataset.

Conclusions: Based on the preliminary results, it appears that novel movement-based interventions (robotic or rhythm) may be an effective training tool to enhance positive affective states in children with ASDs. If our hypotheses are upheld, we will be providing objective evidence supporting the efficacy of embodied movement interventions for addressing the behavioral and affective impairments of children with autism.

**176.118 118** Efficacy of a Facial Emotion Training Program for Children and Teens with ASD. B. Evans-Smith*, N. M. Russo-Ponsaran, J. Russo, J. K. Johnson and C. McKown, *Rush University Medical Center*

Background:

Some children with autism spectrum disorders (ASD) have difficulty interpreting others feelings and expressing their own through facial expressions (Klin, A., Sparrow, S. et al, 1999). They may not direct their visual attention to important facial features that convey emotional information (Moore, Heavey, & Reidy, 2012), struggle to process rapid stimuli (Rump, K., Giovannelli, J., et al, 2009), and have difficulty expressing emotion with their faces (Yirmiya, et al., 1989). The authors developed the Facial Emotion Training Program which incorporated methods to address these challenges unique to current treatment programs (Russo-Ponsaran, Evans-Smith, et al., 2013).

Objectives:

Our main objective was to demonstrate that children who participated in this training program would improve in recognition (speed and accuracy) and self-expression of facial emotion relative to a wait list control group. A secondary objective was to evaluate skill generalization.

Methods:

Twenty-five high-functioning, verbal children with ASD (mean age = 11.1 years, range 8-15 years; mean IQ 99.8+20) who demonstrated a facial emotion recognition deficit were block randomized to an active intervention or waitlist control group. The intervention was a modification of a commercially available computerized facial emotion training tool, the MiX™ by Humintell, which uses dynamic adult faces. The modifications addressed the special learning needs of individuals with ASD which included: coach-assistance, a combination of didactic instruction for seven basic emotions, repeated practice with increased presentation speeds, guided attention to relevant facial cues, and imitation of expressions. Training occurred twice a week for approximately 45-60 minutes across an average of six sessions. Outcome measures assessed (1) dynamic affect recognition with the MiX™ and Child and Adolescent Social Perception Scale (CASP), (2) static affect recognition with the CATS, DANVA2, NEPSY II Affect Recognition subtest; (3) self-expression (coded videotape); and (4) social functioning with parent-report on the Emory Dyssemia Index and Vineland Interpersonal Relations subscale prior to and after treatment.

Results:

A series of ANCOVA's were run to assess between group differences, controlling for full scale IQ, age, autism severity, and pre-test ability for each measure. Pre-test values between the active intervention and waitlist control groups were not significant. Analyses with emotion recognition measures indicated highly significant main effects for the MiX, DANVA2, and NEPSYII ($p<.05$, all comparisons) immediately following training. Coding for the CASP is currently underway. There were no between group differences for parent-report of social functioning. Self-expression significantly improved after training ($p=.001$). Paired t-tests for within group comparisons were also significant for most recognition measures: MiX, DANVA2, NEPSYII, and CATS 3 Faces; the parent report, Emory Dyssemia Index Facial Expression and Nonverbal Receptivity subscales ($p<.05$); and for self-expression ($p<.000$).

Conclusions:

The Facial Emotion Training Program enabled children and teens with ASD to more accurately and quickly identify feelings in facial expressions with stimuli from both the training tool and generalization measures and demonstrate improved self-expression with their faces. Anecdotal reports from parents also indicated

increased awareness to emotions in daily interactions.

**176.119 119** Evaluating Social Motivation As a Predictor of Change in Loneliness in the Context of Individualized Treatment. R. Elias*, A. Trubanova and S. W. White, *Virginia Polytechnic Institute and State University*

Background:

Young adults who have Autism Spectrum Disorder (ASD) without co-occurring cognitive deficits often encounter marked interpersonal difficulties within the university setting. As adolescents with ASD develop, many become more aware of their social difficulties. Despite an increase in the number of students with ASD enrolled in universities, there currently is no empirically-supported intervention designed to target the social needs of college students with ASD. The social difficulties that university students with ASD present with can lead to social isolation and loneliness. Children and adolescents with ASD report higher levels of loneliness when compared to typically developing (TD) peers (Bauminger & Kasari, 2000; Lasgaard, Nielsen, Eriksen, & Goossens, 2010). Individualized social intervention in the university setting may promote changes in loneliness symptoms among a young adult ASD sample.

Objectives:

It is possible that young adults who are more motivated to socially engage with others will experience more loneliness, especially in the college milieu. This study evaluated social motivation as a predictor of change in loneliness in the context of individualized treatment.

Methods:

Data from a preliminary randomized controlled trial (RCT) are analyzed. The trial will be complete in late April of 2014, so we will have data analyses completed by the conference. Eight students with a previous diagnosis of ASD, confirmed by the ADOS-2 (Lord et al., 2000) and a clinical interview were recruited to participate in this ongoing study. Participants were randomly assigned to one of two pilot interventions. Young adults participating in the College and Living Success (CLS) intervention ($n$=4) receive individual therapy with a trained graduate clinician, social outings in the campus community, and supportive coaching all on a weekly basis. The CLS intervention targets emotion-regulation, anxiety, social-integration, and skills of daily living. Students participating in the Brain Computer Interface (BCI) program ($n$=4) practice social interaction and interpreting emotional facial expressions in a virtual reality setting on a desktop computer. During baseline evaluation and upon completion of the interventions, students complete measures of social motivation (Social Responsiveness Scale-2-Adult Self-Report; Constantino & Gruber, 2005) and loneliness (UCLA Loneliness Scale Version 3; Russell, 1996).

Results:

The sample was predominantly male ($n$= 5) with age ranging from 18-23 years (M=20.95), and estimated Verbal IQ ranging from 86-136 (M = 120.33). Self-report measures of loneliness and social motivation from baseline to endpoint will be assessed using reliable change index scores (Jacobson & Truax, 1991).

Conclusions:

The potential implications for the study are twofold. First, if the CLS or BCI intervention programs are efficacious at minimizing loneliness symptoms in college students with ASD, the results may inform future intervention tested with larger sample sizes. Second, if social motivation is identified as a predictor of loneliness symptoms, this may elucidate benefits or weaknesses in interventions which target motivating social involvement.

**176.120 120** Examining the Effects of Compass on the Self-Efficacy of Teachers of Students with Autism. A. D. Rodgers*[1], L. A. Ruble[1], W. H. Wong[2] and J. H. McGrew[3], (1)*University of Kentucky*, (2)*The University of Kentucky*, (3)*Indiana University - Purdue University Indianapolis*

Background: Self-efficacy is described as confidence in one's ability to complete task demands (Bandura, 1997). Self-efficacy is associated with higher degree of effort, willingness to endure hardships, and ability to manage difficult situations. Self-efficacy is of particular interest to implementation science researchers because of the importance of understanding why evidence-based practices fail to be implemented in community settings. For this study, the self-efficacy of classroom teachers of students with autism spectrum disorders (ASD) was investigated. The Autism Self-Efficacy Scale

for Teachers (ASSET) is a new measure for special educators of students with ASD. The ASSET is a 30-item questionnaire based on a 100-pt scale with excellent internal consistency (alpha = .96). Research shows the ASSET correlates negatively correlated with teacher stress (Ruble, Toland, Birdwhistell, McGrew & Usher, 2013), a significant issue that often leads to burnout and eventual attrition. Little is known about teacher self-efficacy and what other variables might be of influence. The ASSET was administered within a larger randomized control trial of a parent-teacher consultation intervention called the Collaborative Model for Promoting Competence and Success (COMPASS).

Objectives: The purpose of this study was twofold: (a) to examine the influences of time (beginning and end of school year) and group assignment (placebo or treatment group) on teacher self-efficacy, and (b) to evaluate the impact of self-efficacy on child goal attainment outcomes.

Methods: Teacher-child dyads were randomly assigned to a placebo control group (PBO) or one of two treatment groups (COMPASS followed by either face-to-face teacher coaching or by web-based teacher coaching). Data were collected at baseline (prior to group assignment) and after the treatment period. A total of 44 special education teachers of children aged three to eight with ASD participated. Of these teachers, 29 were in the experimental group and 15 were in the PBO. An analysis of covariance was used to measure the effect of time and group on ASSET scores. Child goal attainment was determined by an independent observer and based on goal attainment scaling (Ruble, Toland, & McGrew, 2012).

Results: At baseline, mean ASSET scores for the PBO was 71.4 (SD = 13.5) and for the experimental group was 76.1 (SD = 11.1); at the end of the school year, mean ASSET scores for the PBO was 77.1 (SD = 11.8) and for the experimental group was 84.4 (SD= 9.3). Analysis of covariance using baseline ASSET scores as the covariate indicated no difference between the two groups on final ASSET scores F(1,41) = .3.4, p = 07, eta squared = .08. There was a small relationship between pre and post ASSET scores as indicated by an eta squared value of .22. More importantly, ASSET scores did not correlate with child goal attainment outcomes for the PBO (r = -.18, p = .52) but did correlate with child goal attainment outcomes for the experimental group (r = .40, p = .03).

Conclusions: Although COMPASS did not have an effect on teacher self-efficacy, the self-efficacy of teachers in the experimental group was associated with child outcomes.

**176.121 121** Examining the Social Outcomes of Practice Based Models of Social Skills Interventions for Children with Autism in Schools. J. J. Locke*[1], E. Rotheram-Fuller[2], C. Kasari[3] and D. S. Mandell[4], (1)*Perelman School of Medicine, University of Pennsylvania*, (2)*Arizona State University*, (3)*University of California Los Angeles*, (4)*University of Pennsylvania School of Medicine*

**Background**: Social impairment is the most challenging core deficit for children with autism spectrum disorder (ASD). They experience challenges in social reciprocity and communication that impede their ability to navigate social interactions, impacting the presence and quality of relationships with peers. These social discrepancies exacerbate with age and if left untreated, continue through adulthood. Several evidence-based interventions address social impairment in children with ASD; however, adoption, use, and implementation of these interventions by schools is challenging.

**Objectives**: The purpose of this study was to compare three groups of children from: a) a district that has adapted and implemented evidence-based social skills programs to support included students with ASD; b) a university-based intervention program for children with ASD that was implemented within the school setting by outside researchers; and c) inclusion only settings.

**Methods**: A total of 92 children with ASD participated in this study. Data were drawn from multiple sources: a) two schools in a school district who adapted and implemented evidence-based social skills interventions for included children with ASD (n = 14); b) a randomized controlled field based trial in 23 schools of a university developed social skills intervention for included children with ASD (n = 45); and c) 16 schools that were not implementing a social skills intervention for participating students with ASD beyond inclusion (n = 33). The average age of students was 8.4 (*SD* = 1.6) years. The majority

was male (88%) and Caucasian (52.2%). Children in the target student's classroom completed sociometric ratings about various groups of children who hang out together in the classroom to determine children's social network centrality. In addition, independent observers watched children on the playground using a time-interval behavior coding system. Observers recorded children's solitary engagement on the playground, and frequency of initiations.

**Results**: Separate linear regression models were used to test for associations between the three groups and each of the social outcomes (i.e. social network centrality, solitary engagement, and number of playground initiations). Compared to children in the university-developed randomized controlled trial, children from the practice-based intervention models had significantly lower social network centrality ($p$ = .05) and solitary engagement ($p$ = .04) but significantly more initiations on the playground ($p$ = .04). Children in the inclusion only settings had significantly lower social network centrality ratings than children in the university-developed intervention ($p$ <.001).

**Conclusions**: These data suggest that different types of intervention strategies that address distinctive domains of social ability may be warranted. These data also suggest that practice-based research models may inform how to bridge the chasm between evidence-based, efficacious interventions and what actually occurs in practice.

**176.122 122** Exploring the Lived Experience of Families in the Social ABCs Parent-Mediated Intervention for Toddlers with Autism Spectrum Disorder. M. E. Fenwick*[1], S. E. Bryson[2], E. Dowds[3], K. Lynch[3], S. Hodgson[4], T. McCormick[5], S. MacWilliam[5] and J. A. Brian[6], (1)*University of Calgary*, (2)*Dalhousie/IWK Health Centre*, (3)*Holland Bloorview Kids Rehabilitation Centre*, (4)*Holland Bloorview Kids Rehabilitation Hospital*, (5)*IWK Health Centre*, (6)*Holland Bloorview Kids Rehab/ University of Toronto*

Background:

Given an increasing ability to diagnose ASD in toddlers, there is an urgent need for cost-effective, sustainable, and effective interventions for this age group. One approach that is gaining traction is the inclusion of primary caregivers as intervention mediators, thus allowing for increased treatment intensity ('dosage') in a naturalistic context. The Social ABCs is a parent-mediated intervention that employs the evidence-based fundamentals of Applied Behaviour Analysis (ABA) through Pivotal Response Treatment (PRT), with adaptations made for the toddler age group. The Social ABCs takes the form of live parent coaching with the goal of improving positive emotion sharing and functional verbal communication, and is currently being evaluated through an RCT design at two Canadian sites (Toronto and Halifax; Bryson & Brian in prep.). There is relatively little systematic research investigating the impact on the family of parent-mediated interventions for young children with Autism Spectrum Disorder (ASD).

Objectives:

The primary objective was to explore the lived experience of families involved in the Social ABCs parent-mediated intervention for toddlers with ASD.

Methods:

Guided by phenomenological inquiry, semi-structured face-to-face interviews were conducted using open-ended questions to address topics relevant to family outcomes of early intervention for children with disabilities. All of the families who had completed the Social ABCs parent-mediated intervention phase in Toronto at the time of recruitment were invited to participate in this follow-up study (n=11). Seven parents (6 mothers, 1 father) from six families participated in the interviews. Of the children with ASD, three were boys, and all were between the ages of 19-33 months at the time of intervention, and between 2 years, 10 months and 4 years, 8 months at the time of the interview. Thematic analysis was used to interpret and understand parents' reported experiences.

Results:

Five major themes emerged: 1) impact on the child, 2) impact on parents, 3) impact on the family system, 4) feasibility of implementation, and 5) reflections on the Social ABCs experience. Themes of child gains in communication and engagement, of parent skill acquisition and increased hopefulness for their child's future, and of family-based changes, including reduced stress and improved family relationships, all reveal the complexity of the impact on the family.

Conclusions:

Findings highlight the variety of ways in which the Social ABCs had an impact on the child, the parent, and the family as a system. Preliminary findings from this study provide a rationale for future research exploring families' experience in parent-mediated interventions. These findings may contribute to the growing evidence base in support of parent-mediated interventions for toddlers with ASD, and may inform practice, policy and program development related to early intervention for young children with ASD and their families.

**176.123 123** Facial Emotion Recognition and Expression Deficits in Children with ASD and the Effects of Training. J. Russo*, B. Evans-Smith and N. M. Russo-Ponsaran, *Rush University Medical Center*

Background: The better one is able to express an emotion, the better one can recognize emotions in others (e.g. Iacoboni & Mazziotta, 2007). Deficits in recognition and expression of facial emotions are common in autism spectrum disorders (ASD). Therefore, we developed a computer and coach assisted facial emotion training program for children with ASD that incorporates both emotion recognition and expression.

Objectives: Utilizing a wait list control (WLC) and active intervention (AI) design, we tested recognition and expression of facial emotions before and after training. Our first objective was to show improvements in recognition and expression accuracy after training. Our second objective was to establish whether there was a trend for specific emotions to be more difficult for children to recognize and express, even after training.

Methods: 21 children with ASD (11=WLC; 10=AI; ages 8-16 years) participated; diagnoses were confirmed with the SCQ, ADI-R, and ADOS. Eligible children demonstrated a facial emotion recognition deficit based on direct assessments. Children were randomly assigned to either the WLC or the AI group. We chose a commercially-available computer program (MiX™ by Humintell) as the primary training tool, but modified it to include coaching assistance to direct children's attention, to coach on expression exercises, and to navigate the program. The program includes seven emotions: anger, disgust, fear, surprise, contempt, joy, and sadness. Before training, children completed the MiX pre-test and were asked to show the seven emotions using their faces. After training, children completed the MiX post-test and again demonstrated each facial expression. Each child in the WLC group was matched with an AI participant and completed pre- and post- testing following the same temporal schedule, but did not receive any intervention until completing the full testing protocol. Performance on the MiX was captured as percent correct for each emotion. Individual emotion expressions were video-recorded and then coded on a scale of 0-2 (0= no movement of their face; 1= attempted display of the emotion; 2= appropriate display of the emotion).

Results: Within the AI group, performance on perception improved significantly from pre- to post-testing for all seven emotions ($p \leq .05$, all comparisons). Similarly, emotion expression was significantly improved from pre- to post-testing for all emotions except fear and sadness within the AI group ($p \leq .05$). WLC children did not have a significant change in performance on either perception or expression at post-test. When rank ordering the difficulty of recognition for each emotion for all children at pre-test, contempt was the most difficult (mean=30%), followed by disgust (mean=33%), fear (mean=46%), sadness (mean=58%), anger (mean=60%), surprise (mean=68%) and finally, joy (mean=83%). Similarly, contempt was the most difficult and joy the easiest emotion to express at pre-test.

Conclusions: Results support the effectiveness of the training program to improve children's perception and expression of facial emotions. Future studies can identify which emotions are particularly difficult for children with ASD, with an eye towards tailoring clinical interventions for a child. Further investigation is needed to draw causal inferences as to the relationship between the mastery of perception and expression.

**176.125 125** Indian Mothers' and Fathers' Changing Views of Their Child with Autism before and after a Parent-Child Training Program. R. S. Brezis*[1], T. Weisner[1], T. C. Daley[2], N. Singhal[3] and M. Barua[3], (1)*UCLA*, (2)*Westat*, (3)*Action For Autism*

**Background**:

The Five-Minute Speech Sample (FMSS; Magana et al., 1986) has been used extensively across different clinical populations and varied cultural

contexts to assess parents' relationship with their child and predict outcomes (Bhugra & McKenzie, 2003; Hooley & Parker, 2006). To our knowledge, this is the first study in any culture to compare the views expressed by mothers and fathers of children with autism using the FMSS method, and to examine the effects of a parent-training intervention on their views.

**Objectives:** (1) What are the themes raised by Indian mothers and fathers of children with autism? (2) In what ways do mothers and fathers differ in the themes they raise, (3) before and after a parent-training intervention?

**Methods**: Forty mothers and fathers were interviewed before and after a 3-month Parent-Child Training Program at Action for Autism (AFA), New Delhi. During the intervention, mothers are taught practical teaching techniques for their child with autism, with a further focus on acceptance and empowerment. Families came from all regions of India, with varying education and SES backgrounds. Children ranged in age from 2.5 to 10, and were mostly low-functioning (ADOS severity range: 6-10). In the FMSS, parents are asked to describe their child and their relationship with their child for 5 uninterrupted minutes without further interviewer comment; if parents pause or stop, the interviewer asks the parent to continue. Interviews were transcribed and translated into English, and coded for emergent themes. Inter-rater reliability of Kappa>.8 was obtained on all topics.

**Results**: Indian parents of children with autism describe their child and their relationship with their child in ways akin to parents of children with autism elsewhere around the globe (Karst & Van Hecke, 2012). Parents' focus is on the unique aspects of their child's behavior, and their attempts to treat and ameliorate symptoms. In describing their child, parents focus primarily on social, cognitive, communication and self-help skills, and less on repetitive behaviors and sensory interests. After the AFA 3-month training program, parents focus less on social skills and challenging behaviors, and are less concerned that their child be 'normal'; they are more concerned with the child's future, employ more autism terminology, and are more likely to reflect on their own role as a parent. Mothers are more likely than fathers to speak about their relationship with their child, and reflect on their role as a parent. Fathers are more likely than mothers to mention their child's future after the parents' death. (McNemar's test; all *p*'s<.05).

**Conclusions:**

The FMSS method provides parent descriptions and concerns about their children without explicit prompts or questions by interviewers. There were differences between mothers and fathers, and changes in themes following the parent-training intervention. Further studies using the FMSS in both high- and low-resource communities in other societies, can help identify parents' shared and unique concerns, and in turn discover associations with parental and children's outcomes.

**176.126 126** Non-Intensive ABA Is Not Superior to Other Intervention Methods in Young Children with Autism Spectrum Disorder. H. Roeyers*, S. Van der Paelt and P. Warreyn, *Ghent University*

Background:

Since age at the start of the treatment is an important predictor of the effect of an intervention in children with autism spectrum disorder (ASD) (McConaghie & Diggle, 2007), it is essential to start the most beneficial treatment as soon as possible. However, the lack of studies that directly compare different intervention methods, makes clear recommendations in favour of a specific method quite difficult. Applied Behaviour Analysis (ABA) is widely recognized as a well-established treatment for ASD. Many controlled studies show gains in language, cognitive and adaptive functioning (see Reichow, 2012; Vismara & Rogers, 2010). It should be noted however that most studies in favour of ABA evaluated very intensive programs, usually of 20 to 40 hours a week. Implementing such programs on a large scale in clinical practice is difficult because of a lack of financial resources and trained staff. Studies with less intensive forms of ABA seem to be less effective (Eldevik, Eikeseth, Jahr, & Smith, 2006). Furthermore most studies have looked primarily at the effects of ABA on cognitive and adaptive abilities. Next to comprehensive interventions like ABA, there is growing attention for specific training programs in social-communicative abilities. These abilities are proposed as important treatment goals because they are considered to be pivotal areas of development. Several researchers have shown that imitation and joint attention abilities of

children with ASD can improve with a specific non-intensive training (Ingersoll, 2010; Kasari, Freeman, & Paparella, 2006; Warreyn & Roeyers, 2013).

Objectives:

The main goal of the present study was to compare the effect of different methods of intervention, used in community settings, on social-communicative abilities in young children with ASD. More specifically an intervention based on ABA was compared with a more specific intervention program targeting imitation and joint attention (I/JA) and with treatment as usual (TAU).

Methods:

85 young children with ASD between 22 and 75 months were divided in three groups according to intervention method: ABA, I/JA and TAU. Intensity of treatment was similar in the three groups and none of the children had more than 6 hours of 1 to 1 treatment a week. Pre- and post (after 6 months) assessments included autism symptom severity, imitation, joint attention, symbolic play and language.

Results:

A repeated measures MANOVA revealed that children in the three groups significantly improved for autism severity, imitation, symbolic play, initiating joint attention and receptive and expressive language. There was no interaction with the type of intervention. Follow-up analyses showed large inter-individual differences in the three groups. Both child and general intervention characteristics were associated with outcome.

Conclusions:

Our results demonstrate that on average there is no difference between the three intervention methods in the amount of progress children make with respect to their social-communicative abilities after a 6-month-period. While a substantial proportion of children made good progress, there was a subgroup that made hardly any progress. This study shows that it is important to focus on "what works for whom" instead of trying to find a one-size-fits-all-treatment for children with ASD.

**176.127 127** Parents Broader Autism Phenotype and Parenting Stress: Comparison Among Mothers of Children with Autism Spectrum Disorders, Down Syndrome and Typically Developing Children.

A. Zaidman-Zait*[1], L. Eichelberg[2] and E. Dromi[3], (1)*University of British Columbia*, (2)*Tel-Aviv University*, (3)*Tel Aviv University*

Background:

Higher levels of parenting stress have been found in parents of children with autism spectrum disorder (ASD) compared to those with other disabilities (Hayes & Watson, 2013). The question remaining is no longer if parents of children with ASD are more stressed than families without ASD, but why are these parents under more stress. Previous studies have identified numerous child variables that are related to increased parenting stress, however, parental predictors that might be related to ASD have been examined less extensively. One parent related factor that may increase the likelihood of experiencing stress is parents' broader autism phenotype (BAP) representing a subclinical set of personality and other features found in relatives of individuals with ASD such as rigidity, aloofness, hypersensitivity to criticism, interpersonal difficulties etc.) thought to index familiarity and/or genetic liability to autism (Piven et al., 1997).

Objectives:

This study sought to examine (1) the presence of the BAP in Israeli mothers of children with ASD, children with Down syndrome (DS), and children with no disabilities (TD); and (2) to examine the associations between parenting stress (using both general and context-specific measures of parenting stress) and parents' BAP scores across the three groups of mothers.

Methods:

Participants included 61 mothers of children with ASD, 19 mothers of children with DS and 43 mothers of TD children. The age of the children ranged from 5 to 9 years (Mean age = 6.9 years, SD = 1.5). Mothers completed the Autism Spectrum Quotient (AQ, Baron-Cohen et al., 2001); the Parenting Stress Index-Short Form (PSI-SF, Abidin, 1995); a modified version of the Family Stress Scale (Quittner et al., 1990); and a family demographic survey. A series of one way ANOVAs and Pearson correlations were conducted.

Results:

ANOVAs analyses indicated that there were no significant differences between the three groups of mothers in AQ total score and on each of the AQ's domains scores (i.e., social skill, attention switching, attention to detail, communication and imagination). Consistent with previous studies, mothers of children with ASD report higher levels of parenting stress compared to mothers of children with DS and TD children ($F(2,120) = 29.49$, $p < .001$; $F(2,120) = 29.74$, $p < .001$ respectively). Inspection of the correlations across the three groups revealed different patterns of associations. For example, whereas in both the DS and TD groups there were significant correlations between the AQ communication and attention domains and the parent-child dysfunctional interaction scale of the PSI ($r = .34$ - $.49$ $p<.05$), no such associations were found among the ASD group.

Conclusions:

While numerous child variables impact parenting stress, mothers' personality and other features representing autistic related traits also significantly affect mothers' experiences of parenting stress. At the same time, these sets of personality and other features have a different influence on the experience of parenting stress among mothers of children with ASD in comparison to mothers of TD children and mothers of children with DS. Providing a potential one of the answers to the question why are these parents under more stress.

**176.128 128** Participant Benefits and Training Opportunities for University Students through a 12-Week Adapted Physical Exercise Program for Adults with Autism and an Intellectual Disability. C. A. Sutherland*, K. Carr, P. McKeen, S. Horton and N. R. Azar, *University of Windsor*

Background: Participating in regular physical activity can produce many health benefits. For individuals with autism spectrum disorder (ASD), exercise can also reduce stereotypical behaviours. However, very few opportunities for fitness training and sport participation are available for these individuals, and a major barrier to participation in formalized exercise programs or sport is the cost. Furthermore, although physical activity guidelines for the general population are readily available, the exercise prescription must be adapted to meet the individual needs of those with ASD and an intellectual disability (ID). Unfortunately, these adaptions are not typically covered in the requirements for a general personal training certification/coursework. Even when the proper education is included, it is rarely accompanied by practical experience with the specific population. Currently, there is a need for the delivery of low-cost exercise programming, by qualified personnel, geared towards adults diagnosed with ASD and an ID.

Objectives: To design an adapted physical exercise (APEX) program for adults with ASD and an ID, which undergraduate and graduate students ("trainers") would deliver free of charge.

Methods: Eleven adults diagnosed with ASD and an ID (age range = 20-61 years; 2 females) participated in a 12-week exercise program. Each participant was paired with a trainer to complete two 90-minute exercise sessions per week. The sessions included a warm-up, a 6-station exercise circuit, sports and games, and a cool-down. Before the start of the program, the trainers received instruction in the areas of adapted exercise technique, progressions and participant interaction. Trainers were required to record the daily exercise routine (sets, repetitions, weight) as well as document their participant's overall progress in a weekly writing assignment. Fitness testing (including a sit-and-reach test for flexibility and grip strength test using a hand dynamometer) was conducted at the beginning, middle, and end of the program, as well as four weeks after the completion of the program to assess retention.

Results: All eleven participants completed the full 12-week program. All participants progressed in terms of repetitions, sets, and weight lifted. Many participants also progressed in terms of skill development (e.g., being able to jump rope or rally with a badminton racket). Eighty percent of the participants showed improved flexibility at the end of the program compared to baseline, but only one of those participants had maintained the improvement at retention. Ninety percent of the participants showed improved maximum grip strength in one or both hands, 70 % of which maintained the improvement at retention. Feedback from the trainers indicated an increased confidence and comfort level in working with these individuals.

Conclusions: The APEX program provided a no-cost opportunity for adults with ASD and an ID to participate in sports/physical activity, while simultaneously providing students with a rare and valuable opportunity to gain hands-on experience in working with these individuals. By the conclusion of the program, all participants made progressions within their program and were able to execute the exercises with proper technique. Improvements in fitness level are possible, but continued engagement is needed in order to retain the improvements.

**176.129 129** Pivotal Response Treatment Increases Processing Efficiency for Social Information. M. Rolison*[1], R. Tillman[1], P. Ventola[1], J. H. Foss-Feig[1], A. Naples[1], H. Friedman[1], D. Oosting[1], L. C. Anderson[2], C. Cordeaux[1], R. Doggett[1], C. E. Mukerji[1], M. Coffman[3], J. Wolf[1], K. A. Pelphrey[1] and J. McPartland[1], (1)*Yale University*, (2)*University of Maryland*, (3)*Virginia Polytechnic Institute and State University*

Background: The social motivation hypothesis of autism proposes that people with autism spectrum disorders (ASD) experience reduced reward for social stimuli, resulting in decreased attention to people, and consequent dysfunction in the developmental specialization of neural mechanisms associated with social behavior. Pivotal response treatment (PRT) is an empirically validated behavioral treatment for ASD that directly targets social motivation to address deficits in interpersonal interaction and communication. Prior work from our group has indicated that a 4-month course of PRT results in measurable changes in pragmatic language, social engagement, and adaptive functioning, with accompanying changes in regional brain activation (Voos et al., 2012). Treatment outcome in terms of neural efficiency has not yet been studied. The current study applies EEG, an imaging method with excellent temporal resolution, to examine the temporal dynamics of the neural mechanisms associated with positive response to intervention.

Objectives: To identify temporal changes in neural mechanisms associated with social perception subsequent to PRT treatment and their association with behavioral outcome measures.

Methods: Five children with ASD between 4 and 6 years of age received PRT for 8 hours per week (6 hours with the child and 2 hours with the parent) for 4 months. Participants completed an EEG session, recorded with a 128-channel Hydrocel Geodesic sensor net, both pre- and post-treatment. During the EEG sessions, participants viewed 73 distinct, computer-generated faces that displayed neutral and fearful expressions. ERPs were segmented to face stimuli and extracted over the right occipitotemporal region. Changes in the amplitude and latency of early feature detection and face-sensitive ERP components (P100 and N170, respectively) were examined. Behavioral outcome was measured using the Autism Diagnostic Observation Schedule (ADOS), Autism Quotient - Child (AQ), Social Responsiveness Scale – Parent Report (SRS), and the Vineland Adaptive Behavior Scales, 2nd edition (VABS-II), which were administered pre- and post-treatment.

Results: Preliminary results reveal decreased N170 latency for neutral face stimuli post-treatment versus pre-treatment ($p$ = .029). There was no significant change in N170 amplitude, or in either P100 latency or amplitude ($p$s > .05). Degree of reduction in N170 latency following PRT was associated with behavioral improvements in social communication skills, as indexed by ADOS and SRS scores.

Conclusions: PRT was associated with normalization of neural indicators of social behavior. Notably, effects were observed at specific markers associated with social perception, rather than low-level sensory processes, suggesting focal treatment effects on social-communicative behavior. These findings provide the first evidence of alterations in processing efficiency resulting from PRT; neural alterations also mirrored degree of behavioral improvement associated with treatment. Study results emphasize the import of brain-based outcome measures acquired with temporally sensitive imaging methods.

**176.130 130** Positive Self-Esteem As a Predictor of Decreased Problem Behaviors in Adolescents with ASD Following the UCLA PEERS® Intervention. D. Diaz*[1], C. Costa[1], J. Hopkins[1], S. Bates[2], M. Cronin[1] and E. A. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience and Human Behavior*, (2)*Pepperdine University*

Background: Individuals with Autism Spectrum Disorder (ASD) are known to have social deficits and elevated problem behaviors (Macintosh & Dissanayake, 2006). Problem behaviors may be categorized as either externalizing (e.g., aggression or hyperactivity/inattention) or internalizing (e.g., social withdrawal, anxiety, or

depression) (Gresham & Kettler, 2010), both of which are frequently observed in youth with ASD (Bauminger et al., 2010). Yet, positive self-esteem or self-concept during adolescence has been found to protect against internalizing and externalizing behaviors in non-clinical samples of adolescents (Piers et al., 2002; Ybrandt, 2008). The Program for the Education and Enrichment of Relational Skills (PEERS®) is an evidence-based, parent-assisted social skills intervention shown to improve social skills and decrease problem behaviors in adolescents with ASD (Laugeson et al., 2009; Laugeson et al., 2012); however, the influence of self-esteem on problem behaviors following this treatment has yet to be investigated.

Objectives: This study examines the extent to which baseline self-esteem predicts decreased problem behaviors in adolescents with ASD following completion of the UCLA PEERS®intervention.

Methods: Eighty-three adolescents with ASD from 11-18 years of age (*M*=14.17*, SD*=1.70) and their parents participated in weekly 90-minute group treatment sessions for 14-weeks as part of the *UCLA PEERS® for Adolescents* social skills intervention. To assess baseline self-esteem, adolescents completed the Piers Harris Self-Concept Scale, Second Edition (PHS-2; Piers et al., 2002) prior to treatment. The PHS-2 includes six subscales measuring self-concept. To assess changes in problem behaviors following treatment, parents completed the Social Skills Improvement System (SSIS; Gresham and Elliot, 2008) pre- and post-intervention. The SSIS assesses problem behaviors including externalizing, bullying, hyperactivity/inattention, internalizing, and autism spectrum problem behaviors. Pearson correlation coefficients were calculated to examine the relationship between baseline PHS-2 and change in SSIS-Problem Behaviors following treatment.

Results: Results indicate that higher baseline standard scores on the PHS-2 Behavioral Subscale significantly predict a decrease in the instances of bullying others per parent report on the SSIS Bullying subscale ($p<.05$) following treatment. In addition, results reveal that higher baseline PHS-2 Behavioral Subscale scores predict a decrease in parent-reported overall problem behaviors on the SSIS Problem Behaviors Scale ($p<.1$) and a decrease in externalizing problem behaviors on the SSIS Externalizing Subscale ($p<.1$) at trend levels following treatment. Results did not reveal any other significant relationships between baseline PHS-2 subscales and change in scores on the SSIS Problem Behaviors subscales.

Conclusions: Findings suggest that adolescents with ASD reporting higher self-esteem prior to treatment may be less likely to exhibit problem behaviors following the PEERS® intervention. In particular, adolescents endorsing more positive behaviors prior to treatment are less likely to engage in bullying behaviors towards others following intervention. Inversely, adolescents endorsing more problematic behaviors prior to treatment are more likely to engage in bullying after intervention. Additionally, greater behavioral problems prior to treatment may result in more externalizing and problem behaviors for adolescents with ASD at a trend level. These findings emphasize the benefit of identifying predictors of treatment outcome to foster the evolution of targeted social skills interventions for adolescents with ASD.

**176.131 131** Social Motivation As a Predictor of Treatment Outcome in Adolescents with ASD Following the School-Based PEERS® Curriculum.

Y. Bolourian*[1], L. Tucci[2] and E. A. Laugeson[1], (1)*UCLA Semel Institute for Neuroscience and Human Behavior*, (2)*The Help Group - UCLA Autism Research Alliance*

Background:

Adolescents with Autism Spectrum Disorder (ASD) present an array of social deficits, which often negatively impact the development and maintenance of friendships. Yet, social skills training during childhood and adolescence may support positive social skills and improve social competence for youth with ASD (Sigman, Ruskin, Arbeile, Corona, Dissanayake, Espinosa, Kim, Lopez, & Zierhut, 1999). The Program for the Education and Enrichment of Relational Skills (PEERS®) is an evidence-based, parent-assisted social skills intervention for socially motivated adolescents with ASD without intellectual disabilities (Laugeson & Frankel, 2010). Implemented in clinical settings, PEERS® targets ecologically valid friendship skills. An adapted version of PEERS® using teacher-facilitation in school settings has also been empirically validated, revealing significant improvements in social skills (Laugeson, 2013). Whereas

adolescents in the parent-assisted program must affirm their desire to participate in treatment, adolescents in the school-based program are not screened for social motivation, potentially impacting treatment outcome.

Objectives:

The purpose of this study is to investigate social motivation as a predictor of treatment outcome in a 14-week teacher-facilitated social skills program (PEERS® School-Based Curriculum) for middle school and high school students with ASD.

Methods:

Under the auspices of The Help Group – UCLA Autism Research Alliance, 146 students with ASD ranging from 12-18 years of age ($M$=15.15, $SD$=1.81) participated in a larger treatment outcome study investigating the effectiveness of the school-based PEERS® curriculum at The Help Group's Village Glen School. Participants received daily social skills instruction in the classroom for 30 minutes, five days per week, for 14 weeks. Instruction was provided by the classroom teachers and teacher aides who were trained and supervised on the intervention.

Treatment outcome measures collected at pre- and post- intervention included parent-reports on the Social Responsiveness Scale (SRS-P; Constantino, 2005), Social Skills Improvement System (SSIS-P; Gresham & Elliot, 2008), and Social Anxiety Scale (SAS-P; La Greca, 1999). Pearson correlations were calculated to examine the relationship between Social Motivation on the SRS-P at baseline and the difference between pre- and post-intervention scores on treatment outcome measures.

Results:

Results reveal that baseline Social Motivation predicts an increase in overall social skills ($p$<.05) on the SSIS-P and in overall social responsiveness ($p$<.01) on the SRS-P. Results also reveal baseline Social Motivation significantly predicts a decrease in internalizing behavior ($p$<.03) on the SSIS-P as well as a decrease in overall social anxiety ($p$<.03) and fears of negative evaluation by others ($p$<.01) on the SAS-P.

Conclusions:

These results suggest that adolescents with ASD who demonstrate greater social motivation and drive to interact with peers prior to treatment using the PEERS® School-Based Curriculum are more likely to increase their social skills and social responsiveness following intervention. Findings also suggest that adolescents who are socially motivated to increase and enrich their peer interactions are likely to exhibit fewer internalizing behaviors, less apprehension about peer evaluations, and decreased social anxiety following intervention. This study appears to be the first to examine the impact of social motivation on treatment outcome in a school-based social skills program for adolescents with ASD.

**176.132 132** Summer Robotics Camp: A Pilot Social/Vocational Intervention for Adolescents with ASD and Their Peers. J. Kaboski*[1], J. Beriont[1], C. R. Crowell[1], M. Villano[1], K. Tang[1], H. Miller[1], T. Crown[1], W. McWherter[1], T. Gorman[1], M. Won[1], J. Zenk[1], K. G. Wier[2] and J. J. Diehl[1], (1)*University of Notre Dame*, (2)*Sonya Ansari Center for Autism and University of Notre Dame*

**Background:** Although adolescents with autism spectrum disorder (ASD) can be academically successful in general education classroom settings, they often experience difficulty making friends, generalizing the social skills that they learn, and maintaining relationships. Such difficulties, if continued into adulthood without intervention, are likely to lead to social isolation, depression, and social anxiety as well as create obstacles to higher education, employment, and personal relationships. For individuals with ASD who have developed the requisite social *skills*, there are limited opportunities to improve social *performance* in supervised settings (Koegel et al., 2012).

**Objectives:** We piloted a weeklong Summer Robotics Camp designed to improve social performance and increase vocational skills in an environment designed to focus on the intrinsic interests of participants, rather than their social difficulties. The program was based on previous work on improving social performance with elementary school age children with ASD by Koegel et al. (2012). The objective of the camp was to increase social/vocational development of individuals with ASD through: (1) a decrease in social anxiety, (2) an increase in social performance, and (3) an increase in robotics knowledge.

**Methods:** We recruited 8 individuals with ASD and 8 typically developing (TD) peers, ages 12-17, who received general education science instruction at school, and who expressed an interest in robotics. ASD diagnoses were independently confirmed using ADOS, SCQ, and clinical judgment. Participants completed a weeklong summer camp, during which they learned robotic facts, actively programmed an interactive robot, and learned "career skills" (e.g., how to work collaboratively). For the programming, individuals worked in pairs (1 ASD: 1 TD) on a programming project that culminated in a presentation in front of campmates and family. Pairs were closely matched on IQ, robotics experience, and age to ensure equal participation in the task. Participants were not labeled as having ASD; social/vocational training was given to all participants regardless of diagnosis. Pre- and post-treatment data were collected on: participant-reported levels of social anxiety (Social Anxiety Scale), parent-reported social skills (Social Skills Improvement System), and a test of participants' knowledge of robotics.

**Results:** A series of paired samples t-test were conducted to compare the baseline data with post-test data. For both ASD and TD groups, there was a significant improvement on the measures of social anxiety ($t$=4.09, $p$<.001) and robotics knowledge ($t$=10.55, $p$<.001). There was no significant improvement on the total scores of parent-reported social skills for either ASD or TD groups ($p$=.57), although it should be noted that the participants came in with the requisite level of social skills.

**Conclusions:** These results provide a preliminary support for the effectiveness of a summer robotics camp at decreasing social anxiety, and improving knowledge of science and robotics in adolescents with ASD. As an unintended benefit, similar improvements were observed in TD individuals suggesting that benefits of this type of program could extend beyond the treatment group. Further study is needed to specifically examine the real-time social *performance* beyond parent-report measures of social *skills* in order to see if there are improvements in social performance.

**176.133 133** Supporting Rural Families with Toddlers on the Autism Spectrum: Understanding Family and Child Characteristics in an Effort to Develop Accessible and Effective Intervention. K. Hume*[1], L. Turner-Brown[2], B. Boyd[2] and C. C. Arnold[2],

(1)*University of North Carolina, Chapel HIll*, (2)*University of North Carolina at Chapel Hill*

Background:

Access to quality early intervention services for toddlers with ASD in rural communities is rare across the country. Family Implemented TEACCH for Toddlers (FITT) was developed as a structured teaching intervention adapted to be developmentally appropriate for toddlers with ASD, and more responsive to needs of rural families in the state of North Carolina. Better understanding of the status and needs of rural families, as well as how intervention translates to these families, will allow researchers and interventionists to more adeptly form community partnerships in rural communities.

Objectives:

(1) Compare the sample of rural and non-rural families through descriptive analysis of demographic data and pre-test scores on a sample of measures; and (2) Compare feasibility and acceptability of FITT for rural versus non-rural families through the analysis of the following data: therapist fidelity, parent adherence, and social validity.

Methods:

Study of the efficacy of FITT on child and family outcomes is ongoing in a three-year randomized control trial which will enroll 60 toddlers with autism and their caregivers who will be randomly assigned to receive FITT or services as usual (SAU). Treatment consists of 24 sessions, 20 90-minute home sessions and four group parent sessions. Complete data is currently available for 23 toddlers and caregivers with an additional 15 anticipated prior to May 2014. In this early analysis of rural and non-rural families, participants include 18 rural families and toddlers with ASD (FITT=13, SAU=5) and 21 non-rural families (FITT=15, SAU=6).

Demographic data related to family variables (e.g., race, maternal age, maternal education, income, household size) were collected at study enrollment, as well as baseline data related to family and child functioning (e.g. Parenting Stress Index, Mullen Scales of Early Learning, ADOS severity score). T-tests and Chi-squared will be

used to examine differences in mean scores across the rural and non-rural sample.

Treatment fidelity and parent adherence data were collected at in-home sessions. In addition, parents completed a social validity rating form upon completion of the full intervention. For the FITT group, T-tests will be used to compare mean scores on each measure across the rural and non-rural sample.

Results:

Rural versus non-rural differences with regard to toddler participants, family characteristics, intervention fidelity, and parental engagement will be presented. Early analysis for the full sample indicate that the intervention is feasible, as treatment fidelity ratings of project interventionists was strong, with average fidelity ratings of 88.3% (range: 58 – 100%) and acceptable, with average parent adherence ratings of 80.8% (range 30-100%). Preliminary analyses indicate significant differences are found in maternal age and maternal education, but not child's age or race, family income, Mullen derived developmental quotient, parental stress, or ADOS Comparison Score. Further analyses will be included.

Conclusions:

Through early analysis of the demographic and pre-test variables of the rural sample, as well as an examination of the feasibility and acceptability of FITT, we aim to better understand the rural context and how FITT may support both access to and participation in early intervention services in rural communities.

**176.134 134** TMS-Based Neuromodulation Improves Functional Measures of Information Processing and Behavioral Responses in Autism Spectrum Disorder. E. M. Sokhadze*, A. S. El-Baz, L. L. Sears and M. F. Casanova, *University of Louisville*

Background:

The study is based on an underlying neuropathology model of autism which emphasizes minicolumnar pathology and lateral inhibition deficits resulting in behavioral and executive dysfunctions. We proposed that neuromodulation based on low frequency repetitive Transcranial Magnetic Stimulation (rTMS) will enhance lateral inhibition through activation of inhibitory double bouquet interneurons and will be accompanied by improvements in the prefrontal executive functions. In addition we proposed that rTMS will improve cortical excitation/inhibition ratio and result in changes manifested in electrocortical responses such as event-related potentials (ERP) and evoked and induced EEG gamma oscillations during cognitive tests.

Objectives:

TMS offers a noninvasive method for altering excitability of the neural circuits and induction of functional reorganization in the cortex. We reported earlier positive effects of rTMS in autism spectrum disorders (ASD) in our pilot studies using shorter 6- and 12-session long rTMS courses. Along with traditional behavioral evaluations in current study we used ERPs and induced gamma responses power and coherence in a visual oddball task with illusory Kanizsa figures. Wee compared clinical, behavioral and elecotrocortical (ERP, single trial EEG) outcomes in 2 groups of children with autism (TMS, wait-list group). We predicted that 18 session long course in ASD patients will have better behavioral and ERP/EEG outcomes as compared to age- and IQ-matched wait-list ASD group.

Methods:

We used 18 sessions of 1Hz rTMS applied bilaterally over the dorso-lateral prefrontal cortex (DLPFC) in 20 individuals with ASD (11-21 yrs old). The wait-list group was comprised of 20 age-matched subjects with ASD tested twice. Both TMS, and wait-list (WTL) groups were assessed at (1) the initial baseline using clinical behavioral questionnaires ( i.e., Aberrant Behavior Checklist [ABC], and Repetitive Behavior Scale-Revised [RBS-R]) and during performance on visual oddball task with Kanizsa illusory figures, and (2) post completion of 18 sessions of TMS (or wait period).

Results:

Post-TMS evaluations showed decreased irritability and hyperactivity on the ABC, and decreased stereotypic behaviors on the RBS-R. Following rTMS course we found decreased magnitude of the

frontal N100 ERP component and evoked gamma power to non-targets, and shorter of the fronto-central P2a and P3a ERPs and reduced induced gamma oscillation power to non-targets in TMS group as compared to the WTL. These ERP changes along with increased P3b and enhanced induced gamma oscillations (higher power, phase coherence) to targets are indicative of more efficient processing of information post-treatment. Enhanced information processing was also reflected in such behavioral response measures as reaction time (RT) and error rate.

Conclusions:

These results could be considered as a replication of our prior studies using shorter rTMS course. Collected data support our concept that rTMS improves executive functioning as evidenced by normalization of ERP and EEG responses and behavioral reactions during executive function test, and also by improvements in clinical behavioral evaluations. The study links behavioral, clinical, and ERP/EEG responses during cognitive tests and TMS outcomes with an underlying developmental neuropathology model derived from investigations in our laboratory.

**176.135 135** The Effects of Robot-Child Interactions on the Solo and Social Synchrony of Children with Autism Spectrum Disorders. M. Kaur*, S. Srinivasan, A. Desrosiers, T. Gifford, K. Marsh and A. N. Bhat, *University of Connecticut*

Background: Children with Autism Spectrum Disorders (ASDs) have significant motor impairments in dual and multilimb coordination as well as imitation and praxis (Green et al., 2008; Fournier et al., 2010). Motor incoordination in this population not only impacts their performance of daily activities but also affects their social participation skills (Bhat et al., 2011).

Objectives: In the present study, we evaluated the efficacy of a novel movement based intervention using robots on the solo and social coordination skills of children with ASDs between 5 and 12 years of age.

Methods: 24 children with ASDs between 5 and 12 years of age were matched on age and level of functioning and randomly assigned to either a robot group or an academic group. Children in both groups received 16 training sessions over 8 weeks (2 sessions per week). Pretest and posttest sessions were conducted in the first and last weeks of the study. The robot group engaged in imitation games involving whole body movements and drumming with a humanoid robot, Nao (Aldebran Robotics, Inc.) and an adult model. The academic group engaged in tabletop academic and fine motor activities such as reading, building, and arts & crafts with an expert trainer and an adult model. Generalized motor performance was examined using the standardized Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) and the Sensory Integration and Praxis Tests (SIPT) in the pretest and posttest. Specifically, we used the bilateral coordination, fine motor precision, and fine motor integration subtests of the BOTMP and the bilateral motor coordination subtest of the SIPT. Training-specific changes in social synchrony between the child with ASD and the adult model were assessed during an early, mid, and late training session using standard rhythmic actions. Specifically, we assessed the percent of time children spent in-phase, anti-phase, and off-synchrony with the model.

Results: Preliminary data from one child with ASD who received robotic training suggest the presence of generalized and training-specific improvements in solo and social synchrony. Specifically, the child improved motor performance on the bilateral coordination subtest of the BOTMP by 18 points and reduced the total number of errors in the SIPT by 16 points in the posttest compared to the pretest. In terms of social synchrony, the child with ASD increased the percent of time spent "in-phase" with the adult model from 14.61% in the early session to 32.27% in the late session. Given the nature of the training activities in the academic group, we hypothesize that children in this group will show greater improvements in the fine motor subtests of the BOTMP post-training compared to the robot group. We are continuing to analyze all the collected data.

Conclusions: Our final results may provide supporting evidence for the use of robot-child interactions within group-based motor activities to improve the solo and social synchrony abilities of children with ASDs and could serve as a promising tool for addressing the motor and social impairments of this population.

**176.136 136** The Impact of Pivotal Response Treatment on the Spoken Language Phase of Preschool Children. H. E. Flanagan[1], E. Gore-Hickman[2] and I. M. Smith*[3], (1)*IWK*

*Health Centre*, (2)*University of Calgary*, (3)*Dalhousie University / IWK Health Centre*

Background: Pivotal Response Treatment (PRT) is a widely used intervention for children with Autism Spectrum Disorders (ASD). Children receiving PRT experience gains on standardized measures of expressive communication that measure vocabulary and grammar skills (e.g., the Preschool Language Scale; Smith et al., 2010). Guidelines recommend exploring the impact of treatments on a wider range of expressive communication skills (e.g., phonology, pragmatics) using approaches that incorporate natural language samples (Tager-Flusberg et al., 2009).

Objectives: To examine the impact of PRT on children's spoken language phase (preverbal communication, first words, word combinations, sentences, or complex language) using a comprehensive approach recommended by an expert panel that combines data from standardized assessment and natural language samples.

Methods: Participants were 16 preschool children who received a year of intensive community-based PRT (15 hours/ week for 6 months; 10 hours/week for 3 months; 5 hours/week for 3 months). Using structured guidelines based on those outlined by Tager-Flusberg et al. (2009), each child's spoken language phase was determined pre- and post- intervention. Categorization incorporated information from video-recorded natural language samples (collected during a play-based task), and standardized measures (Preschool Language Scale, 2nd ed. and Vineland Adaptive Behavior Scales, 2nded.).

Results: Many children (44%) advanced one language phase (e.g., from first words to word combinations), and 11% advanced two phases (from preverbal to word combinations). Children who were preverbal at the start of intervention were less likely to move to a higher phase (11% attained first words; 22% advanced to word combinations). Additional analyses explored gains in specific language domains (e.g., vocabulary, pragmatics).

Conclusions: Most children receiving PRT in a community program experienced gains on a global measure of spoken language phase. Outcomes varied across language domains and initial skill levels. Determining gains in language phase may be useful across a range of clinical and research contexts.

**176.137 137** Ummeed Parent Program for Autism (UPPA) - a Culturally Appropriate Parent-Mediated Intervention Program for Parents of Children with Autism in Mumbai, India. K. Sengupta* and V. Krishnamurthy, *Ummeed Child Development Center*

**Background:** Parent mediated programs to teach social communication to children with autism are important for LMIC countries like India where there is a huge discrepancy between requirement for and access to services. Few models of parent mediated interventions exist that are applicable in the context of a resource poor setting viz India.

**Objectives:** To identify challenges in the implementation of an existing parent mediated intervention program& to develop an intervention appropriate for the Indian setting by incorporating modifications to address the challenges.

**Methods:** 70 families with children with autism participated in a manualised, parent mediated program (*Teaching Social Communication to Children with Autism* by Ingersoll & Dvortcsak, 2010; Ingersoll & Dvortcsak,2006; Ingersoll & Wainer, in press). Parents were trained to increase child's engagement, attention, awareness and initiations through group lectures, video clips, modelling, therapist guided parent-child interaction, and home-work.

Initial challenges included high rates of parent attrition due to time commitment, requiring reduction of duration from the original 12 to 5 weeks. Second, challenges of language and low levels of literacy necessitated translation of lectures and parent handouts from the original English into Hindi. While original concepts were all retained, terminologies used were simplified along with inclusion of more informal teaching methods like modelling and hands-on demonstrations. Third, lack of caregiver awareness about autism as a condition in general and its associated developmental and behavioural challenges in specific often took away the focus from key teaching areas during therapist mediated parent child interaction sessions and was addressed by addition of a psychoeducational component at the beginning of the program . Fourth, traditional hierarchical family structures often hindered

effective implementation of strategies at home. Extended family members, in particular the paternal grandparents, were actively encouraged to attend and participate in didactic as well as therapist mediated sessions. Fifth, financial challenges due to lack of state funding was countered by external funding and provision of child care facilities at the center itself.

**Results**: Post program assessment showed that Indian caregivers found the program comprehensible and applicable (on 5 point Likert scales, Understanding how to use techniques at home μ = 4.8; Clear, understandable, helpful coaching μ = 4.7). Parents appeared more confident of playing and interacting with their child (μ=4.3), implementing strategies at home (μ=4.6), and helping other family members to engage with their child (μ=4.2). Parent perception of their child's skills (Increase in Social engagement μ = 4.4, Improvement in communication and language skills μ = 4.6) showed significant benefits. Parent statements at the end of the program consistently reported better engagement, as well as improvement in their children's ability to communicate.

**Conclusions:** UPPA is a unique, culturally appropriate, parent mediated intervention, targeted towards increasing social communication for families with children with autism in LMIC countries that merits further study. Future directions for research include conducting long term follow up of participating families as well as documenting and manualising of the modified format to facilitate training of trainers such as community workers for its use in similar settings across LMIC countries.

**176.139 139** Vocational and Personal Independence Training for Individuals with Autism Spectrum Disorder: Effectiveness of the Practical Assessment Exploration System (PAES). A. D. Smith*, A. W. McCrimmon and S. Cairns, *University of Calgary*

Background: Currently, there are no specific, validated vocational training programs for individuals with autism spectrum disorder (ASD). As children with ASD transition into young adulthood, developmentally appropriate interventions must occur to facilitate increased independent functioning (Seltzer, Shattuck, Abbeduto, & Greenberg, 2004). The Practical Assessment Exploration System (PAES; Swisher, Green, & Tollefson, 1999) is a functional vocational skills training tool that teaches and measures vocational potential in individuals with disabilities. This research investigated the efficacy of the PAES program in the ASD population, with specific attention paid to vocational and independence training.

Objectives: Although the development and implementation of targeted vocational programs for individuals with ASD is important, empirical support for such intervention is limited. The PAES program, with its emphasis on the development of vocational skills and behaviours in individuals with developmental disabilities, can be considered an efficacious intervention program for the ASD population. This project sought to evaluate the PAES program in the context of adolescents and adults with ASD; provide a comprehensive understanding of improvements in vocational skills, social skills, and employment interests; and indicate suggestions for program improvement for the ASD population.

Methods: The final sample of participants included 12 adolescents or young adults diagnosed with ASD. As there are no standardized assessment tools designed to evaluate improvement in vocational ability, a mixed-methods approach was utilized to gather information on vocational skills, cognitive and adaptive abilities, and social skills in adolescents and young adults with ASD. Interview data was also gathered on perceptions of program strengths, weaknesses, and suggestions for program improvements from program attendees, parents/guardians, and program facilitators. The Wilcoxon Signed-Rank Test was used to compare attendee performance on quantitative measures before and after intervention. Thematic analysis was used to analyze and report themes found within the qualitative interview data, to facilitate a deeper understanding of participant perspectives.

Results: In general, both the quantitative and qualitative results of this study provide convergent preliminary support for the PAES program in enhancing the vocational and related skills of adolescents and adults with ASD. Specifically, a statistically significant change in performance was displayed on the TEACCH Transition Assessment Profile (TTAP) vocational skills and vocational behaviour subtests indicating that attendees improved their vocational skill and behaviour after participating in the PAES program. Interviews with parents, facilitators, and

attendees highlighted four primary themes: strengths, benefits derived, limitations, and program suggestions. These results, taken together with quantitative improvements in vocational skills and behaviours, suggest that attending PAES is associated with the improvement of vocational skills for adolescents and adults with ASD.

Conclusions: It is the case that vocational research in relation to an ASD population has been quite limited. The present research has underscored the importance of an adolescent and adult emphasis. The preliminary evidence indicates that attendees' performance on the TTAP was improved subsequent to completion of the PAES program, thus providing an indication of the program's efficacy in improving the vocational abilities and behaviours of adolescents and young adults with ASD.

## 177 Specific Interventions - Pharmacologic

**177.140 140** Patterns of Psychotropic Medication Use Among Children Referred for Autism Spectrum Disorder Evaluation. I. Bukelis*, F. J. Biasini, K. C. Guest, S. E. O'Kelley, A. N. Harris and A. Patel, *University of Alabama at Birmingham*

**Background:** About 30-60% of individuals with Autism Spectrum Disorder (ASD) take psychotropic medications, and there is also evidence that many children are prescribed these medications even before they receive an ASD diagnosis (Aman et al., 2005 and Mandell et al., 2008). National trends in psychotropic polypharmacy among children increased from 22% (1996-1999) to 32% (2004-2007) (Comer et al., 2010). Little is known about the specific types of medications individuals with ASD are getting before ASD diagnosis.

**Objectives**: To determine prevalence and type of psychotropic medication use in a tertiary care clinic sample of children referred for Autism Spectrum Disorder (ASD) diagnostic evaluation.

**Methods:** Retrospective cohort study of 585 children (mean age 5 years, range 1.4 - 17.5 years) who received ASD diagnostic evaluation and intellectual evaluation at an interdisciplinary clinic between 2006 and 2009. Records regarding psychotropic medication use prior to formal ASD diagnostic evaluation and insurance status were reviewed for each participant.

**Results:** Of the 585 participants, 54% met criteria for ASD (52% with autism, 39% with PDD-NOS, and 9% with Asperger syndrome) based on evaluations utilizing the ADOS, ADI-R, and clinical opinion. The leading diagnoses in non-spectrum group (NS) (46%) were communication disorder (30%), developmental disorder or intellectual disability (22%), and multiple developmental and/or behavioral diagnoses (34%). Eighty three percent of the sample was male and 68% was white non-Hispanic. Mean FSIQ for participants was 80.8 (range 31-126). Within our sample, 23.4% were taking psychotropic medications (18.5% in ASD group and 29% in NS group) prior to diagnostic evaluation and of these, 12% had already tried more than one class of psychotropic medications (10% in ASD group and 15% in NS group) before the formal ASD evaluation; 17% tried stimulants (13.4% in ASD group and 20% in NS group) and 10% of participants had tried atypical antipsychotics (9% in ASD group and 10% in NS group). In the current study, 51% of participants were covered by Medicaid and 40% were covered by private insurance.

**Conclusions**: Psychotropic medication use is common among young children with and without

**177.141 141** Modulation of the Locus Coeruleus-Noradrenergic System with Milnacipran Vs Placebo in Autism Spectrum Disorder. R. H. Noone*[1], C. J. Ferretti[1], B. P. Taylor[2], E. Racine[1], J. L. Kirsch[1] and E. Hollander[3], (1)*Montefiore Medical Center, Albert Einstein College of Medicine*, (2)*Montefiore Medical Center/Albert Einstein College of Medicine*, (3)*Albert Einstein College of Medicine*

Background: Developmental dysfunction of the locus coeruleus/noradrenergic (LC-NA) system has been proposed as a possible cause of autism spectrum disorders (ASD). Anecdotal parent reports, clinical observations and formal studies have found that up to 40% of children with ASD experience improvement of autistic behavior during fever, which may provide clues to the pathophysiology and potential therapeutic interventions for ASD. Accordingly, we posit that the dramatic fluctuations in behavioral states observed during febrile episodes suggest the involvement of the LC-NA system, a widespread and versatile neuromodulatory system that we suggest is common to febrigenesis and the modulation of autistic behaviors. Milnacipran (MLN) is predominantly a norepinephrine reuptake inhibitor that may enhance function of the LC-NA system. We hypothesize that MLN will re-activate the LC-NA system in patients with autism in a fashion similar to that seen with fever, thus resulting in improvement in attention, irritability, repetitive behaviors and social cognition.

Objectives: To determine whether MLN improves attention dysfunction, irritability, repetitive behaviors and social cognition in patients with autism.

Methods: A 12 week randomized, double-blind, placebo-controlled trial of MLN up to 200mg/ was performed in subjects aged 18 – 50 with a DSM-IV TR ASD diagnosis, confirmed by ADI-R and ADOS. Comorbid medical, neurological and psychiatric illnesses with the exception of ADHD and OCD were excluded. Conners Adults ADHD Rating Scale-Observer Version (CAARS-O), Aberrant Behavior Checklist (ABC), and Clinical Global Impressions Improvement Scale (CGI-I) were measured.

Results: Interim analyses revealed clinically meaningful improvement on milnacipran versus placebo in CGI-I, CAARS-O Inattention/Memory Hyperactivity/Restlessness, Problems with self-concept, DSM-IV Inattentive Symptoms, ADHD Symptoms Total and ADHD Index. Improvements

on milnacipran versus placebo were also observed on the ABC Irritability, Stereotypy, and Hyperactivity subscales. No significant differences between treatment groups were found on the CAARS Impulsivity/Emotional Lability and DSM-IV Hyperactive-Impulsive Symptoms subscales or the ABC-Social Withdrawal or Inappropriate Speech subscales.

Conclusions: Treatment with MLN versus placebo produced clinically meaningful improvements in several domains of the core symptoms of ASD. We posit that this was accomplished via activation of the LC-NA system by MLN mimicking the effects of fever, however more research is needed.

**177.142 142** Multi-Site Randomised Controlled Trial of Fluoxetine in Children and Adolescents with Autism (FAB): Rationale and Design. A. Mouti*[1], M. Kohn[1], D. Reddihough[2], C. Marraffa[3], P. Hazell[4], J. Wray[5], K. Lee[2], P. J. Santosh[6], S. Reid[3], D. Dossetor[1], N. Silove[1], J. Carlin[3], A. Whitehouse[7], J. Granich[7], S. Kloprogge[3], M. O'Sullivan[3], F. Orsini[3], P. Lockhart[3], S. Clarke[1] and A. Poulton[4], (1)*Sydney Children's Hospital Network*, (2)*Department of Paediatrics, University of Melbourne*, (3)*Murdoch Childrens Research Institute*, (4)*Sydney Medical School, The University of Sydney*, (5)*State Child Development Centre*, (6)*King's College London*, (7)*Telethon Institute for Child Health Research, The University of Western Australia*

**Background:** Serotonin reuptake inhibitors (SSRIs) are commonly prescribed 'off -label' for children with autism despite caution regarding their use. To date, clinical trials examining the use of SSRIs in autism have been limited by small sample sizes and inconclusive results. The efficacy and safety of SSRIs for moderating repetitive stereotyped mannerisms in children with autism is yet to be examined. The aims of the FAB study are:

1. To determine the efficacy of low- dose fluoxetine compared to placebo, for reducing the frequency and severity of restricted, repetitive and stereotypic behaviours in children and adolescents with an Autism Spectrum Disorder (ASD).

2. To assess the safety of using low- dose fluoxetine.

3. To explore the relationship between the effectiveness of low- dose fluoxetine and the serotonin transporter genotype.

**Objectives:** To describe the rationale and methodology of the FAB study and a summary of the patient profiles to date.

**Methods:** The FAB study is a multi-site randomized controlled trial. As at October 2013, fifty- eight participants (52 males) aged between 8- 17 years with a confirmed DSM-IV-TR diagnosis of ASD have been recruited. Recruitment is expected to continue until early 2014. Following pre- assessment, eligible participants were randomised to either placebo or active fluoxetine groups. Medication was titrated upwards over a four-week period. Reponses to medication were monitored on a weekly/fortnightly basis using the Clinical Global Impressions Scale (CGI). The primary outcome measure is the Children's Yale-Brown Obsessive Compulsive Scale- Modified for Pervasive Developmental Disorders (CYBOCS-PDD) at 16 weeks. Secondary outcome measures include the Aberrant Behaviour Scale (ABC), Spence Children's Anxiety Scale Parent version (SCAS-P) and the Repetitive Behaviours Scale (RBS-R) also at 16 weeks. Participants were also invited to undergo genetic testing for SLC6A4 allele variants via a cheek swab. The primary outcome (total score on the CYBOCS-PDD at 16 weeks) will be compared for the active and placebo groups using unadjusted linear regression. Secondary outcomes will also be compared using unadjusted linear regression with proportions compared using unadjusted logistic regression.

**Results:** N/A

**Conclusions:** The FAB study is the first clinical trial to specifically investigate the efficacy and safety of low dose fluoxetine for restricted, repetitive and stereotyped behaviours in children with ASD.

**Funding:** The study is funded by a National Health and Medical Research Council (NHMRC 607332) grant by the Australian Government. All study- related expenses including publication costs for manuscripts are to be covered by this grant.

**Competing Interests:** Philip Hazell and Michael Kohn have received payment from Eli Lilly (the manufacturer of fluoxetine) for participation in consultancies, advisory boards, speaker's bureau, and the conduct of clinical trials.

**177.143 143** Preliminary Investigation of Lithium for Mood Disorder Symptoms in Children with Autism Spectrum Disorder. M. Siegel*[1], C. A. Beresford[2], O. Teer[1], M. Bunker[1], M. Verdi[1], A. Stedman[1] and K. A. Smith[3], (1)*Spring Harbor Hospital*, (2)*Children's Hospital Colorado*, (3)*Maine Medical Center Research Institute*

Background: Children with Autism Spectrum Disorder (ASD) have higher rates of co-morbid psychiatric illness, including mood disorders, than the general child population (Leyfer, 2006). Numerous medications have been studied in individuals with ASD, yet only risperidone and aripiprazole (both atypical antipsychotics) have established evidence of efficacy, both for the treatment of irritability (Siegel, 2012). While many children with ASD may experience irritability (aggression, self-injury and tantrums), a small portion also experience symptoms that are typical of a mood disorder, such as euphoria/elevated mood, mania, hyper-sexuality, paranoia or decreased need for sleep.
Despite lithium's established efficacy in controlling mood symptoms in the neuro-typical population, lithium has been almost unstudied in children with ASD.

Objectives: The primary objective of the current study was to describe a subset of children with ASD who received lithium in order to assess potential target symptoms, safety and tolerability. The secondary objective was to examine the relationship between mood disorder symptoms and clinician-rated global improvement scores.

Methods: A retrospective chart review of thirty children diagnosed with ASD by DSM-IV TR criteria and prescribed lithium was conducted at two specialized inpatient psychiatry units. Data included demographics, verbal ability, symptoms prior to lithium treatment, treatment duration and lithium blood levels. Clinical Global Impression of Improvement (CGI-I) ratings were performed by two board certified child psychiatrists with expertise in ASD (MS, CB). CGI-I scores were categorized into either "improved" (CGI-I score of 1 or 2) or "not improved" (CGI-I score ≥3). Data were systematically abstracted by research assistants at each site and sent to the primary site for analysis. The study was approved by the Institutional Review Boards of Maine Medical Center and Children's Hospital Colorado.

Results: Patients were an average of 13.6 (SD=4.1) years old, and primarily male (76.7%), Caucasian (96.7%), and Non-Hispanic (93.3%). All 30 patients were diagnosed with ASD, 10% had a seizure disorder, 56.7% had intellectual disability, and 76.7% were verbally fluent. The mean lithium blood level was 0.70 mEq/L (SD=0.26, Range=0.30-1.20) and the average length of lithium treatment was 29.7 days (SD=23.9, range=4-92). Forty-three percent of of patients were rated as improved on the CGI-I. Independent t-tests indicated that patients who had improved on the CGI-I had a higher number of mood disorder symptoms ($M$=1.38, $SD$=1.26) than those who were not improved ($M$=0.57, $SD$=0.76), $t$=-2.01, $p$=0.058. The presence of mania or euphoria/elevated mood were the symptoms most closely associated with a CGI-I improved rating, but were non-significant, $p$=0.06 and $p$=0.088 respectively. Forty-seven percent of patients were reported to have "any" side effect, the most common of which were vomiting (13%), tremor (10%), fatigue (10%), irritability (7%) and enuresis (7%).

Conclusions: This preliminary exploration of lithium in children with ASD suggests that lithium may be a medication of interest for those who exhibit two or more mood disorder symptoms, particularly mania or euphoria/elevated mood. A relatively high side effect rate merits caution. These results are limited by the retrospective, uncontrolled study design. Future study of lithium in a prospective trial with treatment sensitive outcome measures may be indicated.

## 178 Characterizing Connectivity in Infants and Toddlers at High-Risk for Autism

*Discussant:* A. C. Evans *McGill University*

*Organizer:* S. Paterson *The Children's Hospital of Philadelphia*

Research involving older children and adults with autism spectrum disorder (ASD) has identified a range of atypicalities in brain structural and functional connectivity. However, little is known about how and when connectivity becomes implicated in the emergence of ASD between 6 and 24 months. These questions are addressed in this panel through multimodal imaging studies encompassing structural and functional connectivity analysis in infants at high risk for ASD and controls. These studies investigate changes in resting state connectivity, and various aspects of diffusion-based structural connectivity and white matter organization via tract-based

morphometry, analysis of network metrics and full brain connectomics, to present a comprehensive characterization of connectivity changes during this critical developmental period. Our data demonstrate that changes in connectivity emerge over this period and parallel the timing of group differences in behavior, with differences in early sensory motor areas apparent at 6 months and higher order brain areas implicated at 12-24 months, as more complex social impairments appear. These studies provide important new information relevant to: 1) understanding underlying neural mechanisms in ASD, 2) very early developmental trajectories that are potential target phenotypes for exploring links to etiology and teasing apart heterogeneity, and 3) early detection and intervention targets.

**178.001** Atypical Corpus Callosum Development Associated with Autism in Infants and Toddlers. J. J. Wolff*[1], T. Soda[2], M. A. Styner[1], J. R. Scotton[1], K. N. Botteron[3], S. Dager[4], H. C. Hazlett[1], R. T. Schultz[5], J. Piven[1] and .. The IBIS Network[6], (1)*University of North Carolina at Chapel Hill*, (2)*Harvard University*, (3)*Washington University School of Medicine in St. Louis*, (4)*University of Washington*, (5)*Children's Hospital of Philadelphia*, (6)*Autism Center of Excellence*

Background: Connecting left and right cerebral hemispheres, the corpus callosum is the largest white matter pathway in the human brain. This connective structure begins to develop prenatally and undergoes rapid change over the first postnatal year of life. Numerous brain imaging studies have suggested that the corpus callosum is relatively smaller in older children and adults with autism spectrum disorder (ASD). However, there are no published studies examining the morphological development of this connective pathway in infants and toddlers.

Objectives: To characterize corpus callosum development among infant siblings at low- and high-familial risk for ASD from 6 to 24 months age using fully automated, reproducible approaches to brain image morphometry.

Methods: Structural magnetic resonance imaging data were collected longitudinally from 254 high-risk infant siblings (by virtue of having an older sibling with ASD) and 101 low-risk controls at 6, 12, and 24 months age. Fifty-four children met criteria for ASD based on clinical best estimate diagnosis at age 2 years, yielding 3 groups (low risk, high-risk non-ASD, and high-risk ASD). An automated, inter-hemispheric connectivity-model-based probabilistic subdivision of the midsagittal T1 image was performed to measure total and regional corpus callosum areas. Following this analysis, corpus callosum thickness was measured across 100 equidistant points using a contour-based model. Data were analyzed using a longitudinal mixed-model approach controlling for site, sex, IQ, and total brain volume.

Results: We found increased corpus callosum area in children with ASD starting at 6 months age ($p$ = .01). Probabilistic subdivision data suggested this difference was attributable to the anterior- and posterior-frontal regions of the corpus callosum. Thickness data revealed increased total thickness in children with ASD starting at 6 months age, $p$ = .0001. FDR corrected comparisons indicated a general pattern of high-risk ASD > high risk non-ASD > low risk controls. As with the area data, this difference was strongest in anterior regions of the corpus callosum, and was most pronounced in the high-risk ASD vs. low-risk control comparison. Although there were no significant effects for group X time, growth curves suggested that differences may diminish over the age interval studied.

Conclusions: In contrast to previous work among older children and adults, our findings suggest that the corpus callosum may be larger in infants who go on to develop ASD. This result was apparent whether or not we controlled for factors including total brain size and sex. The contrast between the current findings with the existing literature may reflect developmental phenomenon. While corpus callosum size in older children is driven in large part by use-dependent myelination and growth of commissural axons, much of early corpus callosum development is characterized by robust axon pruning. In this regard, the present findings are consistent with theory and related findings specific to connectivity in very young children with ASD.

**178.002** SVM Classifies Age but Not Autism Risk Using fcMRI Data from 6 and 12-Month-Old Infants at Low and High Genetic Risk for Autism. J. R. Pruett*[1], S. K. Hoertel[1], S. Kandala[1], A. Z. Snyder[1], J. T. Elison[2], T. Nishino[1], E. J. Feczko[3], N. U. Dosenbach[1], B. Nardos[1], J. D. Power[1], B. Adeyemo[1], K. N. Botteron[1], R. C. McKinstry[1], A. C. Evans[4], H. C. Hazlett[5], S. Dager[6], S. J. Paterson[7], R. T. Schultz[7], D. L. Collins[4], V. S. Fonov[4], M. A. Styner[5], G. Gerig[8], S. Das[9], P. Kostopoulos[9], J. N. Constantino[1], .. The IBIS Network[10], S. E. Petersen[1], B. L. Schlaggar[1] and J. Piven[5], (1)*Washington University School of Medicine*, (2)*University of Minnesota*, (3)*Emory University*, (4)*McGill University*, (5)*University of North Carolina at Chapel Hill*, (6)*University of Washington*, (7)*The Children's Hospital of*

*Philadelphia*, (8)*University of Utah*, (9)*Montreal Neurological Institute, McGill University*, (10)*Infant Brain Imaging Study*

Background: Human large-scale functional brain networks are hypothesized to undergo significant changes during development. Little is known about the timing of these functional architectural reorganizations, and there have only been a few infant functional brain imaging studies. Other recent and seminal reports of developmental change in functional brain networks have been called into question because of appreciation of motion artifact effects on resting-state functional connectivity magnetic resonance imaging (fcMRI) data.

Objectives: To address an important part of this developmental question, we made multivariate pattern classifications of fcMRI data acquired in on-going, multi-site, longitudinal studies of brain and behavioral development in infants at low and high genetic risk for autism spectrum disorder (ASD).

Methods: The sample included six and 12-month low- (control) and high-risk (older sibling with ASD) infants *not* meeting clinical best estimate criteria for ASD at 24 months. fcMRI data were processed according to recent analytic and motion cleaning recommendations (Power et al., 2013) with infant-specific adaptations to initial registration and nuisance regression steps. fcMRI matrices were constructed using 230 (from 264 in Power et al., 2011 plus 16 additionally derived from Philip et al., 2012) functionally-defined seed regions which trained image analysts agreed were appropriately positioned in grey matter at both ages. Support vector machine (SVM) methods involved recent adaptations of those used by some of the authors (Dosenbach et al., 2010). 64 datasets from each risk group were pseudo-randomly selected from a total of 164 to allow for balanced, two-group classifications. SVM steps included t test filtering to 200 features, linear kernel, soft margin separation, and leave-one-out-cross-validation (within group). Data from low-risk subjects were then classified with the high-risk-trained SVMs and vice-versa. Control tests accounted for mixed cross-sectional and longitudinal data groupings. Results from data pre-processed using age-specific atlases were compared against results from the same data pre-processed using a cross-age target atlas intermediary. Sensitivities and specificities were measured, and significance was assessed in reference to binomial probabilities. The classification vector from a 128 dataset run allowed visualization of contributing functional connections and seeds.

Results: SVMs classified six versus 12 month-old infants based on fcMRI data, alone: high-risk – accuracy = 75%, sensitivity = 81.3%, specificity = 68.8%, p = 1.22e-05; low-risk – accuracy = 81.3%, sensitivity = 78.1%, specificity = 84.4%, p = 5.03e-08. SVMs could not classify genetic risk for ASD at either age – all p > 0.05. The classification vector illustrates contributions from functional connections between regions which *in adults*would populate default mode, somatosensory-motor, cingulo-opercular, and visual networks. Though not exclusive, weights show a pattern whereby stronger functional connections for longer-distance, anterior-posterior functional connections contribute more to classification of 12 months, and those for posterior, left-right functional connections contribute more to classification of six months.

Conclusions: Results support the developmental hypothesis of significant change in functional brain organization with age, here, during a six month period in the first year of life. Findings encourage other basic developmental examinations and pursuit of questions about functional brain network differences associated with ASD.

**178.003** White-Matter Network Inefficiencies in ASD at 24 Months. J. D. Lewis*[1], A. C. Evans[1], J. R. Pruett[2], K. N. Botteron[2], L. Zwaigenbaum[3], A. M. Estes[4], G. Gerig[5], D. L. Collins[1], P. Kostopoulos[6], R. C. McKinstry[2], S. Dager[4], S. J. Paterson[7], R. T. Schultz[7], M. A. Styner[8], H. C. Hazlett[8], J. Piven[8] and .. The IBIS Network[9], (1)*McGill University*, (2)*Washington University School of Medicine*, (3)*University of Alberta*, (4)*University of Washington*, (5)*University of Utah*, (6)*Montreal Neurological Institute*, (7)*The Children's Hospital of Philadelphia*, (8)*University of North Carolina at Chapel Hill*, (9)*Autism Center of Excellence*

Background: Autism Spectrum Disorder (ASD) is a developmental disorder defined by behavioural symptoms that emerge during the first years of life, and begin to stabilize by 24 months. Recent research has indicated that abnormalities in connectivity may contribute to behavioural symptoms. However, this research is equivocal with respect to both the nature of connectivity abnormalities and the regions in which they occur,

and currently provides little insight into their early developmental origins. Studies have reported different mixtures of over- and under-connectivity. Critically, most samples have included participants far past the age of onset of the defining behaviours, so many of the reported abnormalities may have resulted from cascade effects of developmentally earlier deviations.

Objectives: To ascertain whether there are abnormalities in connectivity in ASD when behaviours defining ASD first become clear, and if so, which parts of the network are involved.

Methods: An analysis of network efficiency, i.e. the capacity to exchange information across a network, was used to assess white-matter connectivity in a sample of 24-month-olds participating in a multi-site study of brain and behavioural development in ASD. The participants were 113 infants at high risk for ASD by virtue of having an older sibling with ASD, and 23 typically developing infants at low-risk. Of the high-risk infants, 31 were classified as ASD based on Autism Diagnostic Observation Schedule (ADOS) scores assessed at 24 months. Structural MRI data were processed with a fully automated pipeline to derive a cortical surface for each subject and overlay a fine-grain cortical parcellation. Diffusion tractography was used to establish the strength of connectivity between regions of this parcellation, and the lengths of those connections. The efficiency of information transfer between each node and all others (global efficiency) was then assessed for each subject, as well as the efficiency of information transfer between the neighbours of each node (local efficiency). Group differences in these two measures were assessed via statistical linear models, controlling for age, sex, and site.

Results: Significantly decreased local and global efficiency was seen over bilateral posterior regions in high-risk ASD infants relative to both low- and high-risk non-ASD infants. Reductions were present in broad regions of the occipital, parietal, and temporal lobes, including primary visual, somatosensory, and auditory areas, as well as associated secondary processing areas. For global efficiency, reductions were also present in Broca's area; otherwise frontal cortex showed no group differences. Reductions in both local and global efficiency were lesser in comparison to high-risk non-ASD infants than low-risk infants, and more left-lateralized. There were no regions showing increased local or global efficiency.

Conclusions: These results suggest delayed myelination and pruning of connectivity, and so delay or deficit in the optimization of network structure. These immature networks show both reduced segregation and reduced capacity to integrate information between regions. The regions implicated are those involved in early processing of auditory, visual, and somatosensory inputs, areas which typically mature early. Findings of frontal lobe abnormalities in older individuals may result from these early inefficiencies in processing sensory inputs.

**178.004** Atypical Unfolding of Early Brain Development in Autism: A Diffusion Tensor Imaging Study of Structural Connectivity and White Matter Organization.

R. Verma*[1], Y. Ghanbari*[1], W. Parker[1], M. Ingalhalikar[1], M. A. Styner[2], G. Gerig[3], J. D. Lewis[4], J. R. Pruett[5], A. M. Estes[6], A. C. Evans[4], S. Das[7], P. Kostopoulos[7], H. C. Hazlett[2], S. J. Paterson[8], J. Pandey[8], H. Gu[9], K. N. Botteron[5], S. Dager[6], R. C. McKinstry[5], R. T. Schultz[8], J. Piven[2] and .. The IBIS Network[10], (1)*University of Pennsylvania*, (2)*University of North Carolina at Chapel Hill*, (3)*University of Utah*, (4)*McGill University*, (5)*Washington University School of Medicine*, (6)*University of Washington*, (7)*Montreal Neurological Institute, McGill University*, (8)*The Children's Hospital of Philadelphia*, (9)*UNC Chapel Hill*, (10)*Autism Center of Excellence*

Background:

Investigating changes in brain connectivity and white matter (WM) integrity in infants who later develop autism spectrum disorder (ASD) should provide important insights into underlying neural mechanisms and early biomarkers at a time when autistic behaviors are first emerging.

Objectives:

This study employed diffusion tensor imaging (DTI) to examine structural connectivity and measures of WM tissue organization like fractional anisotropy (FA) and mean diffusivity (MD), prospectively, in male infants at high familial risk for ASD (who did and did not meet clinical best-estimate (CBE) criteria for ASD at 24 months (HR+ and HR-, respectively) and non-familial low risk controls (LR-), who did not meet CBE criteria for ASD, at 6, 12 and 24 months of age.

Methods:

DTI data was acquired on 160 HR and 55 LR infants at 6, 12 and 24 months, including 42 HR+ and 118 HR- subjects classified with and without ASD, respectively, at 24 months. Images were registered to a population-specific atlas, subject-wise FA and MD images were created and a linear regression model was fitted per voxel with age, group, and age-by-group interaction incorporated and corrected for multiple comparisons. Automated full brain streamline tracking was constrained with a 314-region parcellation to create a 314x314 connectome, with inter-regional connectivity quantified by the number of connecting fibers, normalized to the template. Connection-wise t-tests on matrices were examined between groups at each age.

Results:

Decreased connectivity was broad spread at 6 and 12 months in HR+ vs. LR-, becoming more specific to decreased long-range connectivity between frontal and posterior regions at 24 months. In concert with decreased long-range connectivity, increased short-range (within-hemisphere) connectivity was observed in HR+ vs. LR- subjects at 24 months. With respect to voxel level measures of WM integrity, HR+ (vs. LR-) subjects had increased MD in right auditory regions of Heschl's gyrus, superior temporal gyrus and the acoustic radiation at 6 months; increased FA in primary somatosensory regions of right postcentral and supramarginal gyri at 12 months; and, increased MD in the left parahippocampal gyrus, hippocampus, supramarginal gyrus, superior temporal gyrus and acoustic radiation at 24 months.

Conclusions:

Using voxel level and connectome analyses, we found patterns of abnormal brain development from 6 to 24 months in HR infants who met CBE criteria for ASD. With voxel level analyses, HR+ showed delayed WM maturation in primary sensory-motor cortices in ASD (regions underlying early information processing) followed by later disorganization of higher order language, learning and memory regions at 24 months. Connectivity analyses showed wide spread decreased connectivity in HR+ at 6 and 12 months of age, but more selective connectivity deficits at 24 months, affecting only long-range connections. Interestingly, at 24 months HR+ showed greater short-range connectivity. However, HR- did not show decreased long or short range-connectivity at any age, suggesting that decreased long-range connectivity by 24 months is critically important to the development of ASD in at-risk infants. Ongoing analyses are looking at relationships between voxel level and connectome measures to improve our understanding of causal mechanisms and develop predictive biomarkers.

## 179 The Role of Environmental Epigenetics in the Etiology of ASDs

*Discussant:* D. G. Amaral *University of California Davis Medical Center*

*Organizer:* M. D. Fallin *Johns Hopkins School of Public Health*

Previous investigations into the etiology of autism spectrum disorders have focused on genetic influences or environmental exposures, independently. The scientific literature has recently recognized the importance of both sources of risk for ASDs, and the potential for gene-environment interaction. However, the mechanism of risk through environmental exposures, and interplay of environmental exposures on gene expression, has largely been unexplored. The purpose of this scientific panel is to present background and new evidence for epigenetic associations with environmental exposures and with ASDs. A primary focus will be on the science of epigenetics, which refers to the many layers of molecular mechanisms that control gene expression, many of which are susceptible to environmental influences. The potential role of epigenetic mechanisms in environmental risk for ASDs, and for mechanisms of gene-environment interaction will be discussed. The panel will specifically cover examples of past and current exposures of concern, mechanisms of epigenetic action, utility of epigenetic signatures for ASD research broadly, and windows of developmental susceptibility–including somatic and germ cell mutations. Speakers will present new findings in epigenetics in ASD and research projects underway, including both human and animal model approaches.

**179.001** Epigenetic signatures at genomic sites sensitive to environmental exposures – potential applications for ASD research. C. Ladd-Acosta*, *Johns Hopkins University*

**Background:** Environmental exposures have recently been shown to play a larger role in autism spectrum disorders (ASD) than previously thought. For example, recent reports have shown prenatal exposure to SSRIs is associated with an increased risk for ASD (Croen *et al.* 2011; Rai *et al.* 2013). Although several lines of evidence suggest a potential role for various prenatal

exposures in risk for ASD, most population-based autism studies lack appropriate and reliable information on prenatal exposure status, making it difficult to assess and definitively determine the relationship between ASD and prenatal exposure status. The field of autism would benefit greatly from having a molecular signature of prenatal exposures, present during childhood, that can serve as a proxy for prenatal exposure when investigating exposure-disease relationships in lieu of having actual prenatal exposure data.

**Objectives:** This talk will provide background on the field of epigenetic epidemiology and its relevance to ASDs. We will then focus on the potential for DNA methylation signatures, present in blood during childhood, that are associated with prenatal exposure to smoking, alcohol, maternal infection, folic acid, select serotonin reuptake inhibitors (SSRIs), and beta-2 adrenergic receptor (B2AR) medications.

**Methods:** Illumina Infinium450 BeadChip arrays were used to measure genome-scale methylation (> 485,000 loci) in blood of 609 children, aged 3-5, enrolled in the Study to Explore Early Development (SEED). Rigorous quality control measures were implemented. Prenatal exposure data were collected via telephone interview with the mother. For each exposure, regression analyses, adjusting for blood cell composition estimates, race, and age, were applied to identify novel sites of altered DNAm associated with exposure.

**Results:** Prenatal exposure data, including dose and timing where possible include active smoking (8%), alcohol (12%), folic acid (90%), B2AR(8%), and SSRI (8%) use as well as infection at any point during pregnancy (29%). Differentially methylated regions and composite signatures for each exposure will be presented. In addition, for prenatal smoking, examination of 26 loci previously shown to have differential methylation by maternal smoking in birth cord blood samples (Joubert et al. 2012), revealed striking concordance in our sample of 3-5 year olds; thus, we examined the persistence of these DNAm changes into childhood. These changes appear to be specific to tobacco exposure since the changes in DNAm at these 26 sites were not replicated when we examined prenatal exposure to infection, alcohol, B2AR or SSRI medications.

**Conclusions:** We show epigenetic signatures of prenatal environments, detectible in early childhood. These blood-derived DNAm measurements thus enable a more feasible sampling source and window for assessment of prenatal exposures for investigating exposure-disease relationships in ASD. This work is funded by the CDC, Autism Speaks, and NIEHS.

**179.002** Epigenetic signatures in ASDs and potential relationship with environmental exposures. M. D. Fallin*, *Johns Hopkins Bloomberg School of Public Health*

**Background:** Epigenetic mechanisms have been suggested in ASDs, particularly given the relationship of epigenetic marks to the environment and to genetic predisposition. However, there have to date been only a few studies of epigenetic marks in humans for ASD research. There is a trade-off between limited post-mortem brain tissue versus available in-life blood samples. Further, these few studies have not integrated genetic and environmental data.

**Objectives:** This presentation will present the existing data for epigenetic associations with ASDs, including both brain and blood-based discovery. We will assess the relationships between brain and blood epigenetic patterns with respect to ASDs and how these relate to environmentally labile genomic regions and to genetic predisposition.

**Methods:** Differential methylation by ASD status was identified in post-mortem brain samples from 19 autism cases and 21 unrelated controls. Differential methylation is also identified in childhood blood samples from 292 cases and 317 controls who participated in the Study to Explore Early Development (SEED). DNA methylation signatures of ASD were compared across tissues from these independent data sets and sampling strategies. Further, available prenatal exposure (from maternal interview) and genome-wide SNP genotype data in the SEED children were examined with the methylation data to characterize the potential genetic versus environmental susceptibility at these specific epigenomic locations.

**Results:** Ladd-Acosta et al. found four regions of the genome to be differentially methylated between autistic cases and controls in a cohort of 41 post-mortem brain tissue samples. We will discuss the use of blood-based data for replication

of these results, as well as the utility in reverse discovery, beginning with blood-based epigenetic signatures, followed by brain. We will then show how these ASD-related signatures relate to prenatal exposures and genetic predisposition.

**Conclusions:** The utility of epigenetic examination of human samples to further our understanding of ASDs will depend on the ability to synthesize rare target tissue data with more abundant surrogate tissue information. This work will demonstrate this point and allow for integration and examination of the relationships between epigenetic signatures and environmental exposures. This work is funded by the CDC, Autism Speaks and NIEHS.

**179.003** Understanding gene/environment interactions through epigenomics. J. M. LaSalle*, *University of California at Davis*

Background: Gene and environmental interactions in autism likely involve a complex "two-way street" in which genetic difference can affect responses to environmental factors, which can in turn impact gene expression through epigenetic mechanisms. The human genome is marked by structural variations including large copy number variations and differences in repetitive sequences. Persistent organic pollutants such as polychlorinated biphenyls (PCBs) can induce DNA hypomethylation and potentially lead to genome instability at repetitive sequences. Chromosome 15q11-13 duplication syndrome (Dup15q) is one of the most common copy number variations observed in autism-spectrum disorders, and a chromosomal locus known to be epigenetically regulated by parental imprinting. Surprisingly, human brain samples with Dup15q syndrome showed significantly higher levels of the persistent organic pollutant PCB-95 than controls or idiopathic autism cases (Mitchell et al., 2012). Furthermore, a genetically susceptible mouse perinatally exposed to the related flame retardant BDE-47 exhibited hypomethylation in brain and reduced sociability compared to controls (Woods et al., 2012).

Objectives: This study was designed to experimentally determine if PCB-95 and/or BDE-47 play a causal or compounding role in DNA methylation differences observed in human Dup15q neurons using epigenomic approaches.

Methods: Human post-mortem brain tissue samples obtained through the Autism Tissue Program were analyzed for PCB levels using mass spectrometry. Tissue was obtained from individuals with autism, IDIC15, or non-affected controls. In addition, Human SH-SY5Y neuroblastoma cells with an additional maternal chromosome 15 were exposed to PCB in vitro to PCB and methylation regions assessed with whole genome bisulfite sequencing.

Results: Human SH-SY5Y neuroblastoma cells containing an additional maternal chromosome 15 (SH-15M)(Meguro-Horike et al., 2011) were used as a cell culture model of Dup15q and PCB-95 interactions. SH-15M cells model the 15q11-13 gene expression and hypomethylation characteristics of Dup15q brain samples that do not act according to copy number, including lower than expected levels of paternally expressed SNRPN and biallelic GABRB3. Whole genome bisulfite sequencing (MethylC-seq) revealed that SH-15M cells exhibited large genomic domains of partial methylation (PMDs)(Schroeder et al., 2013; Schroeder et al., 2011) that were gained in SH-15M compared to parental SH-SY5Y cells and compounded by PCB-95 exposure. There was an enrichment of genes on 15q11-13 affected by PCB-95 exposure in SH-15M cells, but additional genes on other chromosomes were also found to be within differential PMDs in SH-15M with and without PCB interactions, including other autism candidate genetic loci.

Conclusions: The combination of a large chromosomal duplication (Dup15q) and exposure to a historical persistent organic pollutant (PCB-95) resulted in complex interactions, detected as large-scale genomic changes to neuronal DNA methylation levels. The potential for "two-way street" interactions between genetic and environmental factors across generations should be considered in future ASD studies.

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**179.004** Understanding the epigenetic consequences of gene/environment interactions through animal models. E. Rissman*, *University of Virginia*

Background: The epigenetics revolution provides mechanisms by which gene transcription can be

modulated by the environment. The focus of this presentation will be to investigate the hypothesis that that certain environmental compounds, specifically, endocrine disruptors, act epigenetically to modify transcription of important neurodevelopmental genes. Two of the most widely used compounds are Bisphenol A (BPA), which increases rigidity and di(2-ethylhexyl) phthalate (DEHP) which enhances flexibility of plastics. Correlational data provide evidence that exposure to one or both of these compounds during gestation is associated with a variety of suboptimal behaviors in children including anxiety, IQ, and executive function (Braun et al., Braun et al., 2013). In addition to direct actions on the developing brain both of these EDCs have transgenerational effects on testes organization (Doyle et al 2013) and behavior (Wolstenholme et al 2012; 2013).

Objectives: In order to establish causal relationships between EDC exposures in utero, and juvenile behavior, we are using a mouse model. We focus on human relevant doses of BPA and DEHP that are consumed by dams during pregnancy. We assess behaviors in juvenile mice that are either the first generation or several generations removed form EDC exposure. In this manner we can make causal statements about gestational exposures to EDCs and behavior.

Methods: Female mice were exposed to BPA-in chow or control chow throughout gestation in one study. In a second study females received , DEHP or vehicle for a week in mid-pregnancy. Sibling pairs were bred to the third generation with no further BPA or DEHP exposure. First (F1) and third (F3) generation juveniles were tested for social interactions, recognition and in the open field in the BPA experiment. In the DEHP study we tested the same behaviors and examined stress responses.

Results: Bisphenol A exposure during gestation increases social interactions in both male and female juvenile mice interacting with adult females confined to a small holding cell, on the other hand BPA-exposed mice are less willing to interact with other juveniles in an unrestrained test. Interestingly 3-4 generations later juvenile mice in the BPA lineage are more interactive in both tasks and fail to distinguish novel from unfamiliar testing partners. Testing of DEHP-exposed mice is going on at the present time with a focus on stress-responses and anxiety. Target genes in brains of BPA linage mice do not exhibit differences in DNA methylation and other mechanisms are under investigation.

Conclusions: Two commonly used EDCs given to mice at low doses during gestation have short and long term effects on behavior and gene expression. How and which neurodevelopmental genes are modified by these compounds has yet to be determined.

## 180 Illuminating the Developmental Neuropathology of ASD

*Discussant:* M. W. State *UCSF*

*Organizer:* N. Sestan *Yale School of Medicine*

Exome sequencing has led to robust identification of genes associated with Autism Spectrum Disorder (ASD), thus offering an unprecedented opportunity to investigate its neuropathology. However, the large number of genes affecting risk and their numerous biological functions challenge conventional genetic methodologies. To overcome this hurdle we integrate recent ASD gene discoveries with genome-wide analysis of gene expression and regulation in the developing human brain to highlight common biological mechanisms leading to ASD. We will present: 1) Gene-discovery from exome sequencing of the Simons Simplex Collection and where these genes converge in their expression in the developing human brain; 2) A novel approach to integrating exome and expression data to greatly accelerate gene discovery; 3) A map of the gene network regulated by CHD8, a chromatin modifier with the best evidence of ASD-associated via loss of function mutations; and 4) Development of zebrafish models to assess hypotheses of neuropathology in vivo. Through integration of psychiatry, neuroscience, genetics, and statistics we present a strategy that uses the genes discovered by exome sequencing to illuminate features of the developmental neuropathology that underlie ASD.

**180.001** Exome-sequencing based gene discovery and systems biology of autism spectrum disorders. S. J. Sanders*[1], A. J. Willsey[1], K. Roeder[2], B. Devlin[3], N. Sestan[4] and M. W. State[1], (1)*UCSF*, (2)*Carnegie Mellon University*, (3)*University of Pittsburgh*, (4)*Yale School of Medicine*

**Background**: *De novo* loss of function (nonsense, canonical splice site, and frameshift) mutations are associated with ASD based on the observation of a higher rate in cases versus unaffected controls via exome-wide analyses. Furthermore, identification of multiple *de novo* LoF mutations in the same gene in unrelated

individuals has emerged as a reliable approach to identifying ASD-associated genes at genome-wide significance. Previously, based on an initial set of nine ASD-associated genes emerging from exome analyses of 1,043 families, we conducted a co-expression analysis, leveraging spatio-temporally rich data from developing human brain, that has identified layer 5/6 glutamatergic neurons in the prefrontal cortex during human mid-fetal development as relevant for ASD pathophysiology.

**Objectives**: To identify additional ASD-associated genes in a hypothesis naïve manner by conducting further whole-exome sequencing, and to use these genes as inputs for an expanded gene co-expression analysis aimed at refining spatio-temporal understanding of ASD pathophysiology.

**Methods**: We present an analysis of whole-exome sequencing of 457 previously un-reported simplex families from the Simons Simplex Collection (SSC), contributing to a combined analysis of 1,500 simplex ASD families. Two detection algorithms are used to identify single nucleotide variants (SNVs) and insertion/deletions (indels) separately. All putative *de novo* LoF mutations are confirmed through PCR and Sanger sequencing. Genes with multiple *de novo* LoF mutations are used as seed genes for co-expression analyses aimed at refining our recently reported spatial and temporal data regarding convergence of ASD related genes in mid-fetal human cortical development.

**Results**: A total of 196 genes were observed to have at least one *de novo* LoF variant in an affected individual. Of these genes, 18 show at least two *de novo* LoF variants in affected individuals. Comparison with the distribution of *de novo* LoF variants in the unaffected siblings demonstrates that the 196 have a >50% probability of being associated with ASD while the 18 genes with multiple LOF mutations have a >95% of being associated with ASD risk. Eight of the 18 genes with multiple *de novo* mutations are novel ASD-associated genes. Co-expression network analysis based on the expanded set of genes validates our previously observed findings pointing to a convergence of ASD-related mutations in layer 5/6 glutamatergic neurons in the prefrontal cortex during mid-fetal development.

**Conclusions**: Ongoing exome sequencing of ASD trios is rapidly expanding the list of ASD-associated genes. Identification of these genes facilitates analyses of the biological systems underlying ASD pathology. The discovery of additional ASD genes and an expanded co-expression network analysis reported here highlights the convergence of ASD genes in deep layer glutamatergic neurons in the prefrontal cortex during mid-fetal development, strengthening this association. As expected, the data also point to additional possible points of spatio-temporal convergence of ASD mutations, underscoring the importance of integrating other gene discovery methods and genomic datasets such as chromatin state and gene regulation.

**180.002** Modeling gene expression and rare sequence variation identifies genes and subnetworks underlying autism risk.

K. Roeder*[1], L. Liu[1], J. Lei[1], S. Sanders[2], J. Willsey[2], M. W. State[3], J. D. Buxbaum[4] and B. Devlin[5], (1)*Carnegie Mellon University*, (2)*Yale University*, (3)*UCSF*, (4)*Seaver Autism Center for Research and Treatment*, (5)*University of Pittsburgh*

Background:

*De novo*, loss-of-function (dnLoF) mutations occur twofold more often in autism spectrum disorder (ASD) probands than their unaffected siblings. Multiple, independent dnLoF mutations in the same gene implicate the gene in risk and hence provide a systematic, albeit arduous path forward for ASD genetics. Willsey et al. (2013) identified brain gene expression networks as meaningful for organization and inter-relationships of ASD genes; and identified the mid-fetal prefrontal and motor-somatosensory neocortex as the region and developmental periods in which these genes tend to coalesce to confer risk to ASD.

Objectives:

Using Brainspan gene expression from this critical nexus and whole-exome sequencing data, we aim to accelerate the search for ASD risk genes and to obtain subnetworks of genes that promote neurobiological assessment of function.

Methods:

We use a novel algorithm, DAWN, to model two kinds of data: rare variants from exome sequence; and gene co-expression in the mid-fetal prefrontal and motor-somatosensory

neocortex. The algorithm casts the ensemble data as a Hidden Markov Random Field in which the graph structure is determined by gene co-expression. The algorithm combines these interrelationships with node-specific observations, namely gene identity, expression, genetic data, and its estimated effect on risk to identify risk genes.

Results:

DAWN identifies novel genes that plausibly affect ASD risk. Validation experiments provide strong evidence that this set contains many true risk genes. Indeed, in the validation experiment DAWN was able to distinguish the genes that will accumulate new *de novo* loss of function mutations better than any existing method.

Conclusions:

Our results implicate neuritic outgrowth, arborization, guidance, and terminal specification of both axons and dendrites, on the basis of genes predicted to affect risk. Thus we hypothesize our results converge on mediation of coordinated neurite development and that risk for ASD arises from disorganized patterns of arborization in addition to the often-described synaptic dysfunction.

**180.003** The CHD8 regulatory network in the developing brain is enriched for ASD risk genes. J. Noonan*[1], J. Cotney[1], S. Reilly[1], R. A. Muhle[2], W. Niu[1] and W. Liu[1], (1)*Yale University School of Medicine*, (2)*Yale Child Study Center*

**Background:**

Gene discovery in autism spectrum disorders by exome sequencing coupled with co-expression analyses have revealed chromatin modification as a significant point of biological convergence. ASD-associated chromatin modifiers and other regulatory genes may directly control other ASD-associated genes and thereby organize pathways and networks that, when perturbed, lead to ASD. To investigate this mechanism, we have undertaken studies to map the regulatory networks of ASD genes during brain development. Here we focus on Chromodomain Helicase DNA binding protein 8 (CHD8), an ATP-dependent chromatin remodeler that exhibits a high number of *de novo* loss of function mutations in unrelated individuals with ASD, strongly supporting a role for this gene in autism pathology. The loss of CHD8 function may result in aberrant expression of downstream target genes required for proper brain patterning, cell fate determination, or other critical neurodevelopmental processes. Characterizing the CHD8 regulatory network in human brain will therefore provide biological insights into the developmental etiology of autism.

**Objectives**:

To elucidate the CHD8 regulatory network via a) chromatin immunoprecipitation coupled with high-throughput sequencing (ChIP-seq) to identify CHD8 target genes in developing brain b) generation of CHD8 regulatory maps by the co-localization of CHD8 binding with active or repressive chromatin marks; c) identification of global changes in gene expression and chromatin marks due to CHD8 depletion using shRNA; and d) examination of the CHD8 target gene networks to determine if previously identified ASD genes are significantly enriched.

**Methods**:

We have mapped CHD8 binding sites in developing brain and human cell lines using ChIP-seq, and have cross-referenced these sites with maps of specific active or repressive histone modifications to identify CHD8-targeted genes and regulatory elements. The genes targeted by CHD8 have been assessed for enrichment of ASD genes by permutation testing. We will evaluate the biological relevance of these binding events using CHD8-specific knockdown using shRNAs followed by global analysis of the transcriptome and histone regulome.

**Results:**

We found that CHD8 gene targets are significantly enriched in ASD genes bearing one or more *de novo* loss of function mutations, and in genes found in ASD-associated spatio-temporal co-expression networks during human brain development. In developing brain and human cell lines, CHD8 is targeted to promoters and regulatory elements that bear active chromatin signatures, with a strong predilection for active promoters.

**Conclusions:**

Identification and analysis of biologically relevant CHD8 binding sites allows for the generation of CHD8 (and therefore likely ASD-associated) regulatory networks, and provides a general framework for characterizing other chromatin and transcription regulating ASD genes. By generating and integrating regulatory networks for multiple ASD genes, we will uncover molecular and biological points of convergence in pathways that contribute to ASD pathophysiology.

**180.004** Functional Analysis of Genes Strongly Associated with Autism Spectrum Disorders in a Zebrafish Model System. E. J. Hoffman*[1], J. M. Fernandez[1], J. Rihel[2], A. J. Giraldez[1] and M. W. State[3], (1)*Yale University*, (2)*University College London*, (3)*UCSF*

**Background:** Whole-exome sequencing has rapidly expanded the list of ASD-associated genes, while co-expression network analysis is beginning to reveal points of spatio-temporal convergence among these genes. Moreover, these new ASD risk genes are elucidating novel biological mechanisms, such as chromatin modification (*CHD8*) and ion channels (*SCN2A*), complementing earlier genetic findings, which implicated cell adhesion molecules and synaptic proteins (e.g. *CNTNAP2*) in the biology of ASD. We expect these biological mechanisms to disrupt common neural pathways leading to an ASD phenotype, yet delineating these neural pathways remains a challenge. Therefore, a critical next step in elucidating ASD neuropathology is the development of *in vivo* models that allow for the visualization and quantitative assessment of neural pathways in the developing CNS.

**Objectives:** To develop zebrafish as a model system for the functional analysis of ASD risk genes. These studies will capitalize on two key advantages of zebrafish: 1) transparent embryos that enable visualization of neural circuits in real time during brain development; and 2) large progenies, which allow for the conduct of quantitative profiling assays and small-molecule chemical screens.

**Methods:** We utilized zinc finger nuclease and transcription activator-like effector nuclease (ZFN, TALEN) technology to target the zebrafish orthologs of the ASD risk genes *CHD8*, *SCN2A*, and *CNTNAP2*. We analyzed the development of axon tracts, along with excitatory and inhibitory neurons during early embryonic stages to correlate these findings with the readout from behavioral assays. Moreover, we conducted large-scale quantitative behavioral profiling in zebrafish knockouts 4-7 days post fertilization (dpf) to characterize differences in the neural circuitry underlying rest-wake activity.

**Results:** Multiple lines of zebrafish knockouts were generated carrying deleterious germline mutations in *CHD8*, *SCN2A*, and *CNTNAP2*. *CNTNAP2* knockouts show subtle abnormalities in axon organization at early developmental stages and disruption of forebrain commissure formation. Furthermore, these *CNTNAP2* knockouts demonstrate increased susceptibility to chemically-induced seizures. *SCN2A* knockouts display motor abnormalities beginning at 4-5 dpf and do not survive past 11 dpf. Preliminary analysis of quantitative behavioral profiling of all knockouts reveals individual behavioral "fingerprints" indicative of significant differences in rest-wake architecture. The identification of such behavioral phenotypes offers a path forward in illuminating the specific neural circuitry that is disrupted in these knockouts.

**Conclusions:** These experiments provide evidence for the strength and feasibility of zebrafish as a tractable model system for the functional analysis of ASD risk genes and for testing specific hypotheses generated from genomic analyses in humans. While ongoing studies will assess excitatory-inhibitory neuron development in knockouts, preliminary evidence suggests these pathways may be disrupted given alterations in the behavioral profiles of knockouts, and in particular, the increased susceptibility of *CNTNAP2* knockouts to drug-induced seizures. We anticipate that our approach of utilizing large-scale quantitative profiling of zebrafish knockouts of ASD genes will allow the testing and discovery of convergent biological mechanisms underlying the pathophysiology of ASD and aid in the identification of novel therapeutic targets.

## 181 New Insights into the Correlates and Processes of Competent Peer Relations during Preschool

*Discussant:* S. Odom *University of North Carolina*

*Organizer:* N. Bauminger *Bar-Ilan University*

In typical development, "peers are necessities, not luxuries" (Hartup, 2009, p. 3), both for well-being and for children's growth of cognitive, linguistic, and social skills. Peer relations (rather than parent-child relations) constitute one of the major known deficits for children with ASD (APA, 2013); yet there is

considerable heterogeneity. Peer relationships lie on a continuum ranging from a compelling lack of awareness of others to relatively intact peer relations. The peer relationship difficulties noted in older children with ASD likely begin early, but these processes during preschool are not well understood. In this symposium we provide novel and broad insight into the process with a focus on language (pragmatic); social-cognitive (Theory of mind and joint attention); emotion (emotion knowledge, regulation, temperamental negativity and effortful control) and neuropsychological (executive function) correlates of competent peer relations. Novel data will be presented that is based on multidimensional assessment procedures, combining semi-structured and spontaneous observations of peer relations, experimental tasks, and parent reports. Better understanding of the beginnings of peer relationships should provide insight into later difficulties and importantly pinpoint targets for early intervention for children with ASD.

**181.001** Friendship and Pragmatic Skills During Spontaneous Peer Conversation. N. Bauminger*[1] and E. Karin[2], (1)*Bar-Ilan University*, (2)*Bar - Ilan University*

Background:

In typical development, early peer talk is crucial for pragmatic development. Peer talk offers children a wide range of opportunities for mutual learning of social-interactive and linguistic skills (Blum-Kulka & Snow, 2004). The pragmatic deficit, reflected in remarkably deficient conversational capabilities, is considered the hallmark of the language deficit in autism spectrum disorder (ASD) (Stefanatos & Baron, 2011); yet, spontaneous peer talk in preschoolers with ASD was rarely explored.

Objectives:

The current study's major aim was to close this knowledge gap about characteristics of the pragmatic deficit in ASD by examining spontaneous peer talk in preschoolers with HFASD versus preschoolers with TYP. We were also interested in learning about the role of the interaction partner as contributing to pragmatic capabilities, due to prior studies ' reports of higher mutual social engagement, responsiveness, and reciprocal verbal exchanges in interactions with friends versus nonfriends (Newcomb & Bagwell, 1995). Thus, we compared peer talk according to the partner's friendship status (friend/nonfriend).

Methods:

We conducted comparative assessment of spontaneous peer talk during 10-minute free-play scenarios in preschoolers with high-functioning ASD (HFASD; $n$=27) versus with typical development ($n$=30). Groups were matched on SES, verbal/nonverbal MA, IQ, and CA. Correlations with CA, IQ, VMA, and NVMA were examined. We compared the two groups' interactions with a friend partner versus a non-friend partner; additionally, in the HFASD group, we examined interactions with a typical partner (mixed dyads) versus a partner with HFASD (non-mixed dyads). Children's conversations were videotaped and coded to tap pragmatic capabilities and conversational quality.

Results:

As predicted, analysis of observed spontaneous peer conversations revealed a more severe pragmatic deficit in HFASD versus more intact pragmatic capabilities in TYP, for almost all of the pragmatic behaviors and conversational quality dimensions. The most severely affected pragmatic behaviors in HFASD included verbal behaviors (e.g., limited reciprocal conversation, unresponsiveness to interlocutor's cues, unusual intonation) and nonverbal social-gesture behaviors (e.g., inappropriate facial expression, poor eye contact and gaze).

However, for preschoolers with HFASD, 30% of specific pragmatic behaviors were more intact in interactions with friends than in interactions with nonfriends, versus only 18.5% of specific behaviors in the TYP group. In HFASD, interactions with friends were characterized by longer reciprocal conversations that were more responsive to the partner's information-seeking and emotional state and were less overly talkative (pragmatic behaviors) than interactions with nonfriends. Moreover, interactions with friends showed less stereotypic discourse and mispronunciations (speech and prosody aspect) as well as more appropriate facial expressions and eye contact (paralinguistic category) than interactions with nonfriends. Thus, altogether, friendship may enable children to converse in a more socially complex and co-regulated way.

Also, children with higher cognitive capabilities, especially in the HFASD group, demonstrated more intact pragmatic capacities

Conclusions:

Despite the robust pragmatic deficit in HFASD, reflected in conversational capabilities, involvement in friendship relationships and high cognitive capabilities were linked to more intact pragmatic capacities. Clinically, emphasizing friendship in early intervention may help elicit more adequate pragmatic capabilities and presumably fuller peer relations in preschoolers with ASD.

**181.002** Friendship and Joint Attention in Preschoolers with ASD. Y. C. Chang*[1] and C. Kasari[2], (1)*UCLA*, (2)*University of California Los Angeles*

Background:

Children with autism spectrum disorder (ASD) have difficulty making friends. Compared to typically-developing children, children with ASD have fewer friendships and their friendships are of lower quality (Bauminger et al., 2008; Kasari, Locke, Gulsrud, Rotheram-Fuller, 2011). Most of these studies examining friendships in children with ASD have focused on elementary and middle-school aged children. Little is known about friendships in younger children with autism, particularly preschool-age.

Objectives:

The current study will examine friendships in preschool children with ASD and explore the role of joint attention in these friendships.

Methods:

Participants included thirty-one fully mainstreamed preschool children (ages 2-5) with ASD. For each participant, two 15-minute school observations were conducted during his/ her free play. These observations were used to capture "friendships" in the preschoolers. Friendship was defined by three criteria used to define friendship in neurotypical preschool children (Howes, 1983): 1) at least 50% of their social initiation attempts were responded to, 2) at least one interval of joint engagement, and 3) at least one positive affective exchange (adapted from Howes, 1983).

The Early Social Communication Scale (ESCS; Mundy et al., 1986) was administered to each participant to assess the child's spontaneous use of joint attention skills.

Results:

Twenty percent of the children in the sample had friendships. Joint engagement was examined between the two groups of children (children with friendships and children without friendships) during free play. Children who had friends were spending significantly more time in joint engagement ($U = 14.00$, $p < .001$), while children without friends were spending more time in parallel play ($t(29) = 5.965$, $p = 0.016$). Despite the differences between the two groups, as a group, children in the study sample spent the most time in solitary play ($M = 33.71$, $SD = 24.43$).

Two independent sample t-tests were also conducted to examine differences in initiations of joint attention between the two groups. There were no differences in joint attention skills between the two groups ($p > .05$). However, 86% of the children with friends (n = 6) displayed high level joint attention skills including pointing and showing, whereas only 50% of the children without friends (n = 12) displayed high level joint attention skills.

Conclusions:

The findings from the current study suggest that children with autism can have friendships at a young age. There were qualitative differences between children who were defined to have friendships compared to children who did not have friends. In general, children who had friends were more engaged and had more joint attention skills. This suggests that early intervention targeting joint attention is critical for this population of children. Joint attention interventions may increase early social communication skills and help foster more meaningful relationships (Lawton & Kasari, 2012; Wong & Kasari, 2012).

**181.003** The Importance of Emotion Regulation Coping Strategies and Emotion Knowledge for Social Competence with Peers in Preschoolers with Autism. L. B. Jahromi* and A. Dimachkie, *Arizona State University*

Background:

In the preschool years, interactions with peers are often emotionally-charged situations. Children's use of effective *coping strategies* in such situations is critical for maintaining positive exchanges and forming enduring relationships

with peers (Eisenberg & Spinrad, 2004). Several emotional prerequisites have been identified for preschoolers' social competence with peers (Denham, et al., 2003), including *knowledge of others' emotions* (Denham, et al., 1990), *emotion regulation* (i.e., the ability to modulate emotional experiences or expressions; Calkins & Mackler, 2011), and children's *temperamental negativity* and *effortful control* (Rothbart, Posner, & Hershey, 1995). There is a need for more work examining how these processes predict social outcomes among children with autism in order to identify the most critical intervention targets for this population.

Objectives:

In an effort to directly inform peer interventions for children with autism, the first goal of our study was to examine the coping strategies employed by preschoolers with autism in emotional situations with peers. Our second goal was to understand the relative importance of emotion knowledge, emotion regulation, and temperamental negativity and effortful control for children's social competence.

Methods:

Participants were 40 children (*M*age = 54.57 months), including 20 children with high functioning autism (HFA) and 20 matched, typical peers with no significant differences in mental age, receptive language, or expressive language. Children's predominant coping strategies in emotional situations were assessed using the Parent's Reports of Children's Reactions (Eisenberg, Fabes, Nyman, Bernzweig, and Pinuelas, 1994). Emotion knowledge was measured using Denham's (1986) Affective Knowledge Puppet Task. Emotion regulation was measured using the Emotion Regulation Checklist (Shields & Cicchetti, 1997). Temperamental effortful control and negativity were assessed with the Child Behavior Questionnaire-SF (Putnam & Rothbart, 2006). Finally, parents reported on children's social competence using the Child Behavior Scale (Ladd & Profilet, 1996) approximately one year later.

Results:

With respect to coping strategies in emotional situations with peers, after controlling for mental age, preschoolers with autism used significantly fewer positive coping strategies (i.e., less support seeking, cognitive restructuring, and instrumental coping, and more aggression) than their matched peers, $t$ (37) = 4.62, $p$ <.001. Diagnostic group differences also emerged in several emotional prerequisites for social competence, even after controlling for receptive language or mental age. Children with autism showed less knowledge of others' emotions in equivocal situations $t$ (37) = 2.75, $p$ = .011, impaired emotion regulation $t$ (37) = 3.13, $p$ = .003, less temperamental effortful control $t$ (37) = 6.47, $p$ <.001, but no difference in temperamental negativity ($p$ > .05). Results of hierarchical multiple regression indicated that, after controlling for mental age, emotion knowledge ($p$ = .046), and emotion regulation ($p$ = .015), emerged as the most significant predictors of children's social competence with peers, $F$ (5, 39) = 7.357, $p$ < .001, $R^2$= .520.

Conclusions:

Our findings point to the importance of targeting emotion regulation, particularly the use of effective coping strategies, as well as an emphasis on knowledge of others' emotions, as critical intervention components to improve the peer interactions of preschoolers with autism.

**181.004** Theory of Mind and Executive Function in Preschoolers with ASD and TYP as a Basis for Competent Peer Relations. Y. Kimhi*[1] and N. Bauminger[2], (1)*Bar Ilan University*, (2)*Bar-Ilan University*

Background:

EF and ToM capabilities are necessary for children's competent social functioning, that include, amongst others, social interaction and the ability to make, and retain, friendships. Children with ASD have difficulties in theory of mind (ToM) and executive function (EF), which may be linked because one domain (EF) affects the other (ToM). Researchers have established links between ToM and EF among typically developing preschoolers, yet, such links in intellectually able preschoolers with ASD (HFASD) were explored in only two studies to date (Pellicano, 2007, 2010). Furthermore, no data is available concerning explanation of false belief preschoolers with HFASD. Research elucidating EF's relations with ToM in general, and with explanation abilities in particular, may advance the conceptualization and

therefore the facilitation of social-cognitive development in ASD.

Objectives:

The current study aimed to expand understanding of ToM capabilities by employing a comprehensive assessment of false-belief explanation skills alongside explanation types (psychological or informative). We compared preschoolers with HFASD versus preschoolers with typical development on two EF abilities (cognitive shifting and planning) and two major ToM capabilities (explanation and prediction) using first-order false-belief tasks (an unexpected-location task and an affective false-belief task) . We also tested the links between EF and ToM and the function of verbal IQ (VIQ) individual contribution to the relations between EF and ToM.

Methods:

Participants included 29 intellectually able preschoolers with ASD and 30 typical preschoolers, aged 3-6 years. EF tasks included planning (Tower of London) and cognitive shifting (FIST) measures. ToM tasks included predicting and explaining affective and location false-belief tasks.

Results:

Significant group differences emerged on most EF and ToM measures, in favor of typically developing children. The in depth study of explanation abilities revealed that for children with ASD, explanation tasks appear to be more difficult than prediction tasks, contrary to children with typical development, who are able to explain false belief prior to prediction, thus rendering explanation an easier task. The robust links found illustrated the relationship between preschooler's planning abilities and their capacity to predict and explain false beliefs whereas the regression analysis showed that planning predicted children's explanation abilities. VIQ added to the explained variance for most of the ToM explanation tasks.

Conclusions:

The present study aimed to shed light on how specific EF mechanisms may be linked with specific ToM mechanisms at the preschool age in HFASD. The novelty of this study lies in its in-depth examination of ToM explanation abilities in HFASD alongside the role of VIQ. The results underscore that the provision of explanations involve complex cognitive abilities (such as planning abilities), and higher verbal skills, both which are complex for children with ASD. If indeed better planning skills and verbal skills can facilitate ToM explanation abilities in children with ASD, then appropriate interventions could directly promote their social abilities both for understanding and for explaining other persons' intentions, beliefs, and behaviors.

## 182 Implementing Group CBT for Youth with ASD and Anxiety in Clinical Settings: Bridging the Research to Practice Gap

*Discussant:* D. Mandell *University of Pennsylvania Perelman School of Medicine*

*Organizer:* J. Reaven *Univ. of Colorado Denver-JFK Partners*

Children with high-functioning autism spectrum disorders (ASD) are at high risk for developing anxiety symptoms. Cognitive behavioral treatments (CBT) are frequently used in the general population with good success to reduce anxiety. Recently published studies have demonstrated significant reductions in anxiety for youth with ASD following modified CBT interventions (Storch et al. 2013). Because the majority of treatment studies have occurred in controlled university settings, generalizability to other settings is limited. The purpose of this symposium is to discuss variables that may increase the adoptability of evidence-based interventions, maximizing success for clinical practice and narrowing the research-to-practice gap. This symposium also addresses barriers to dissemination of evidenced-based intervention that target anxiety symptoms in youth with ASD, and identifies approaches to fostering the adoption of empirically supported programs for youth with ASD in real-world settings. Four sites were trained in the Facing Your Fears (FYF) program (Reaven et al., 2011) and have implemented the treatment. Session topics include: 1) measurement of anxiety in youth with ASD, with an emphasis on real-world application; 2) mediators of treatment related to implementation; 3) factors that influence the adoption of evidenced-based interventions in clinical settings; and 4) balance between treatment fidelity and model adaptations.

**182.001** Assessing Anxiety and Measuring Treatment Outcomes: Challenges and Creative Solutions for Implementing the Facing Your Fears Program in a Tertiary Care Setting. M. McConnell*[1], K. McFee[1], M. Soltys[1], K. Johnston[2] and G. Iarocci[2], (1)*British Columbia Children's Hospital*, (2)*Simon Fraser University*

**Background:** Children with autism spectrum disorders (ASD) experience greater levels of anxiety than typically developing children, making accurate assessment and diagnosis especially important in this population. Moreover, early assessment promotes early intervention, which is well-known to improve outcomes. However, considerable challenges exist with current measures of anxiety in terms of their clinical utility for children with ASD and in terms of their applicability in real-world clinical settings. Available measures of anxiety have been designed for typically developing children and rely heavily on language and abstract concepts (e.g., emotions and cognitions). Since language impairment and difficulties with abstract thinking are core features of autism, there are important questions about the applicability of traditional measures of anxiety for children with ASD. Likewise, gold-standard anxiety assessment protocols (e.g., *Anxiety Disorders Interview Schedule; Silverman & Albano, 1996)* were developed for use in research settings with typically developing children, and considerable challenges exist when clinicians attempt to apply traditional assessment measures with this special population in real-world clinical settings.

**Objectives:** The primary objective of this presentation is to discuss challenges and possible solutions for assessing anxiety and treatment outcomes in the context of evidence-based intervention for anxiety in children with ASD in real-world clinical settings. Strengths and weaknesses of existing measures of anxiety commonly used with this population will be reviewed, along with their applicability in clinical settings. Factors that complicate assessment of anxiety in the context of ASD, particularly in a tertiary care setting, will be reviewed. Finally, creative solutions and alternative methods of real-world measurement of anxiety in ASD will be discussed, including presentation of two newly-developed visual measures of anxiety designed specifically for children with ASD.

**Methods**: A well-characterized sample of 13 children with ASD and anxiety, ages 8-12, participated in the study. Two visual measures of anxiety were designed for children with ASD participating in the Facing Your Fears program. The first measure, *About My Worry*, uses visual scales to assess children's perceptions of the *frequency* and *intensity* of anxiety symptoms. The second measure, *How My Body Feels*, uses diagrams in conjunction with a visual scale to assess severity of physiological symptoms of anxiety. Traditional measures of children's anxiety (e.g., *Anxiety Disorders Interview Schedule*, *Spence Children's Anxiety Scale*– parent and child versions) were also administered. Data were collected within a repeated-measures, pre-post treatment design in a tertiary care setting.

**Results**: Preliminary findings will be presented with respect to the validity of these visual measures for assessing anxiety in children with ASD, including descriptive and correlational data gathered in a tertiary-care setting.

**Conclusions:** Measurement issues present a significant barrier to implementation of evidence-based assessment and treatments for children with co-morbid mental health issues and ASD receiving services in real-world clinical settings. There is a need for creative solutions to overcoming these barriers as we develop a better understanding of how to best assess anxiety and treatment outcomes for children with ASD.

**182.002** Factors That Influence the Adoption of Evidenced-Based Interventions in Clinical Settings. T. Beattie*[1], A. Sullivan[1] and I. M. Smith[2], (1)*IWK Health Centre*, (2)*Dalhousie University / IWK Health Centre*

**Background:** Children with Autism Spectrum Disorder (ASD) are at increased risk for developing mental health disorders (Kerns & Kendall, 2012). Reaven and colleagues (2011) developed a CBT program for children with ASD and anxiety called Facing Your Fears (FYF). After establishing the initial efficacy of FYF, Reaven et al. (submitted) investigated the portability of FYF to a new clinical setting. FYF was initially implemented at the IWK Health Centre, a tertiary level children's health centre in Nova Scotia, Canada. Initial training in FYF entailed a 2-day workshop followed by review of videotaped sessions by the program developers and bi-directional discussions regarding delivery of content and program development. Initial results yielded strong adherence to treatment fidelity and significant reductions in youth anxiety.

**Objectives:** To examine factors that influence the adoption of the FYF program in a new clinical setting.

**Methods**: In the 2 years following the research implementation phase of FYF, the treatment program continued to be delivered at IWK. Two of the originally trained facilitators trained two additional facilitators; a well characterized sample of 13 children (5 girls, 8 boys, aged 7-12 years) with ASD and clinical anxiety have participated in FYF groups. All child and parent participants completed the Screen for Anxiety Related Disorders (SCARED; Birmaher et al., 1995) pre-post intervention and parents completed the Social Responsiveness Scale (SRS; Constantino, 2005) pre-post. In addition, attitudes and impressions regarding the implementation and long term adoption of FYF were obtained from administrators, group facilitators, and child/parent participants to examine whether it would be appropriate to continue to deliver FYF to youth with ASD and anxiety at IWK.

**Results:** FYF has been designated as the primary intervention approach for children with ASD and anxiety at the IWK Health Centre based on both qualitative as well as quantitative results. Factors that have influenced the adoption process included overall feasibility, ease of implementation and training of new facilitators, and relative advantage of the FYF program compared with existing treatment approaches. Positive treatment outcomes for the youth participants have also influenced the decision-making. Potential barriers to implementation of FYF included challenges in conducting baseline assessments to determine goodness-of-fit to the treatment approach, managing heterogeneous group composition, and working within time constraints to train new facilitators.

**Conclusions:** Many interventions available in community settings for children with ASD have not been empirically validated (Stahmer et al. 2005). It is important not only to consider the efficacy of a treatment program, but the feasibility of implementing and maintaining an effective intervention program in community settings where resources are scarce (Dingfelder & Mandell, 2011). The rising rates of ASD have pressured community service providers to find creative, but also evidence-based, ways to address the mental health needs of this population. The implementation of the FYF program at the IWK Health Centre illustrates how the research-to-practice gap can be narrowed with collaboration between researchers and community clinicians.

**182.003** Factors that Mediate Effective Treatment (CBT) of Anxiety in Children with Autism Spectrum Disorders: Lessons Learned and Potential Impact on Implementation in New Settings.

I. E. Drmic*[1], J. A. Weiss[2], P. Szatmari[3], E. Anagnostou[1], A. Solish[1] and J. A. Brian[4], (1)*Holland Bloorview Kids Rehabilitation Hospital*, (2)*York University*, (3)*University of Toronto*, (4)*Holland Bloorview Kids Rehab/ University of Toronto*

**Background:** Anxiety disorders are the most commonly reported concurrent diagnoses in individuals with autism spectrum disorders (ASD; White et al., 2009); however, there is a paucity of information examining the factors that might contribute to or underlie anxiety. Studies examining the use of cognitive behavioral therapy (CBT) to treat anxiety in ASD have recently begun to receive empirical attention (Lang et al., 2010). Although results are promising, CBT is not effective for all children with ASD. Review of previous treatment research shows significant reductions in parent reported anxiety symptoms after delivery of CBT; however, approximately one third of children still had clinically significant levels of anxiety. In order to improve treatment effectiveness, examination of mediational processes is essential to ensure that we understand how and why treatments work.

**Objectives:** The current study investigates mechanisms that mediate treatment responsiveness of children with ASD receiving CBT for anxiety. This is a pilot study to assess feasibility and variance in the mediator and outcome variables to calculate sample size requirements for a larger, randomized control trial study.

**Methods:** Literature examining mediators and moderators of CBT will be reviewed and discussed in the context of the current pilot project. Twenty-one participants (from 6 groups of approximately 5 children each) with ASD (IQ>70) and their parent(s) participated in a group CBT program for individuals with ASD, Facing Your Fears (i.e., Reaven et al., 2009). Groups were run at Chedoke Hospital, York University and Holland Bloorview Kids Rehabilitation Hospital. Participants were recruited from referrals from clinicians and advertisements on autism-related websites. The current pilot project examined four potential mediators of therapeutic effectiveness: cognitive (i.e., executive function-EF & attentional flexibility), social (i.e., social skills/awareness), parental/family (i.e., family functioning & parental stress), and therapeutic variables (i.e., support &

therapeutic alliance). Measures of anxiety and potential mediators were administered pre-treatment, at two time points during treatment, and immediately and at 4-6 months post-treatment.

**Results:** We have completed data collection across all phases of this project, and are currently assessing how change in child anxiety is explained by changes in the child, family, and interpersonal factors. The CBT groups were run in university settings as a research project, as well as a clinical setting where the added research component was optional. Implementation of measures to assess the various mediators was challenging given the frequency of assessments, but this process presented with unique challenges in the clinical (versus research) context, which will be addressed.

**Conclusions:** There is a tremendously high need for services for individuals with ASD, and yet there are very few public services for this group, as they often 'fall through the cracks' in our mental health care system, thus improving treatments is a priority. It is important to expand our understanding about the underlying mechanisms of change in order help guide treatment programs in effectively addressing these issues and understanding factors that may support implementation in new settings.

**182.004** Implementing the Facing Your Fears Program in Clinical Settings: Balancing Treatment Fidelity and Model Adaptation. J. Reaven*, A. Blakeley-Smith, E. Moody, J. Stern and S. L. Hepburn, *JFK Partners/University of Colorado School of Medicine*

**Background:** Anxiety disorders frequently co-occur in youth with high-functioning autism spectrum disorders (ASD) (Leyfer et al. 2006; van Steensel et al. 2011). Cognitive-behavioral treatments (CBT) are well-established, evidenced-based treatments and have been used in youth with ASD in well-controlled research settings with encouraging results (Reaven et al. 2012; Storch et al. 2013). However, little research exists on the implementation and dissemination of these treatments beyond research settings. Furthermore, little is known about the variables that enhance the ultimate adoption of new interventions to real-world settings. The balance between treatment fidelity and flexible adaptations of treatment models may be critical to understand as evidenced based interventions are disseminated into community settings (McHugh et al. 2009). Successful adoption of new interventions may be most likely to occur when clinicians implement interventions long after training has ended and strong treatment fidelity (without drift) is maintained (Beidas et al. 2011; Carroll, 2013).

**Objectives:** 1) to train mental health clinicians to deliver Facing Your Fears (FYF), a group CBT program for youth with ASD and anxiety; 2) examine the relationship between treatment fidelity and model adaptation in an effectiveness trial; and 3) to determine whether clinicians trained in FYF maintain high treatment fidelity more than two years post-training.

**Methods:** Clinicians (e.g., psychologists/psychologists-in-training) participated in a 2 day training on the FYF intervention. A well-characterized sample of 16 children ages 8-14 (and their parents) participated in the study. Four 14-week group cohorts for children and their families were conducted. Treatment fidelity was examined and acceptability data obtained from all participants, which was incorporated into a revised version of FYF. Preliminary treatment outcome data was obtained for the 16 youth participants. In addition, treatment fidelity will also be examined in a FYF cohort conducted more than 2 years following the training workshop to assess drift.

**Results**: Excellent treatment fidelity was obtained following participation in the original study (87%-95%; M=92%). Acceptability data was collected across all cohorts and specific suggestions for changes in treatment delivery were incorporated into revisions of the FYF program to increase adoptability of program by clinical settings. Preliminary treatment outcome data indicated significant decreases in parent reported anxiety (SCARED), and 54% of the sample demonstrated clinically meaningful improvement for primary anxiety diagnoses. Long-term treatment fidelity will be examined for the cohort conducted 2 years post-training.

**Conclusions:** Results indicated that clinicians new to FYF demonstrated strong treatment fidelity post-training and consultation. Preliminary efficacy data demonstrates corresponding reductions in anxiety for youth participants. An examination of the relationship between

treatment fidelity, model adaptations and long-term sustainability of FYF for new clinical settings will be discussed. Further, key characteristics of the FYF program will be presented on dimensions such as *relative advantage*, (perception that FYF is better than existing interventions) *compatibility* (the extent to which FYF is compatible with a new settings' values and priorities) and *complexity (*perceived difficulty of the FYF to deliver*)* (Dingfelder & Mandell, 2011). Broader implications for dissemination of evidenced based programs will be explored.

## 183 Making Sense of the Links Between Sex Differences and Autism: From Biology to Behavior

*Discussant:* S. Baron-Cohen *University of Cambridge*

*Organizer:* M. C. Lai *University of Cambridge*

The male-bias in the prevalence of autism has two major implications for understanding the emergence of autism. First, studies into mechanisms associated with the development of typical sexual differentiation may provide insight into the etiologies and development of autism. Second, identifying similarities and differences between males and females with autism can inform us about shared characteristics and mechanisms central to the emergence of autism, as well as sex-specific and/or sex-linked characteristics, etiological mechanisms, susceptibility and protective factors. This Scientific Panel brings together research from 4 different groups addressing these two inter-linked themes. The first two presentations discuss how sex-differential gene expression and associated regulatory mechanisms are potentially related to the genetic and epigenetic etiologies of autism. The second two presentations compare and contrast girls and boys, women and men with autism, integrating across levels of brain structure, neural activation, cognition and behaviors. The discussant will address the implications from the interaction of both threads of research, as well as future directions elucidating the links between sex differences and autism.

**183.001** Sex-Differential Gene Expression in Human Brain: Implications for Autism Spectrum Disorders. D. M. Werling*[1], N. N. Parikshak[1] and D. H. Geschwind[2], (1)*University of California, Los Angeles*, (2)*UCLA*

Background: Autism spectrum disorders (ASDs) show a consistently male-biased prevalence, and while genetic factors are known to influence ASD risk, the mechanism(s) by which genetic variants interact with sex-differential biology to exacerbate risk in males and attenuate risk in females is incompletely understood. Gene expression in the brain provides an intermediate phenotype between causal risk factors and the sex-biased presentation of neuropsychiatric disorders, and so the analysis of sex-differential expression patterns may elucidate key pathways influencing sex-biased risk.

Objectives: We aimed to identify and characterize sex-differential gene expression patterns in neurotypical human brain in order to evaluate whether the male bias in ASD prevalence may be driven by differential expression (DE) of ASD risk genes in male and female brain, or whether sex-differential factors act in downstream or interacting pathways to modulate the effects of genetic variants.

Methods: RNA-sequencing data from the BrainSpan project from post-mortem human cerebral cortex at two developmental stages, prenatal (12-22 post-conception weeks; n=14, 7 females) and adult (19-40 years; n=8, 4 females), was processed and analyzed for sex-differential expression using LIMMA. Genes DE by sex (sex-DE) with a minimum fold difference of 1.2 and p-value<0.005 were then compared with sets of ASD-implicated genes, genes differentially expressed in ASD brain tissue, neural cell type markers, and other functionally annotated gene sets from the literature.

Results: We identify over 800 sex-DE genes from both sex chromosomes and autosomes, with a greater number of genes expressed more highly in male than in female cortex. We observe no enrichment of ASD-implicated risk genes among sex-DE genes from either the prenatal or the adult stage. In contrast, among genes up-regulated in male adult cortex, we do find significant enrichment of an up-regulated, ASD-associated co-expression module (M16) identified in post-mortem ASD brain (Voineagu et al., 2011); this module is enriched in astrocyte and microglia markers. Furthermore, sex-DE genes that are also members of the M16 module show parallel up-regulation, with higher expression levels in males versus females and in ASD cases versus controls. Beyond the M16 module, we find that genes that are significantly DE by sex and DE in ASD show concordant directionality and function: genes up-regulated in neurotypical males and ASD mark astrocyte and other glial function, and genes up-regulated in neurotypical females and down-regulated in ASD mark neuronal function.

Conclusions: Our findings suggest that sex-differential ASD risk may not be driven by sex-differential expression of genes carrying currently identified risk variants, but may instead be related to downstream modulation of the effects of genetic risk variants by neuron-glial interactions.

**183.002** Sex Hormone-Mediated Regulation of RORA, a Potential Contributor to Sex Bias in ASD. V. Hu*[1] and T. Sarachana[2], (1)*The George Washington University School of Medicine and Health Sciences*, (2)*Chulalongkorn University*

Background: Expression of retinoic acid-related orphan receptor alpha (RORA) is reduced in both brain and lymphoblastoid cells from multiple cohorts of individuals with ASD. Moreover, RORA regulates the gene for aromatase, which converts male to female hormones that, in turn, regulate *RORA* in opposite directions, with androgen suppressing *RORA.* The regulatory feedback interactions between RORA, aromatase and sex hormones suggest that sexually dimorphic regulation of *RORA* may contribute to the male bias of ASD. However, the molecular mechanisms through which androgen and estrogen differentially regulate *RORA* are still unknown, as are the mechanisms through which RORA deficiency may contribute to the neuropathology of ASD.

Objectives: 1) To investigate the mechanisms involved in the opposite regulation of *RORA* by male and female hormones, including the involvement of hormone receptors, coregulators, and epigenetic changes; 2) To identify genome-wide transcriptional targets of RORA in order to determine relevance to ASD; 3) To investigate sexually dimorphic expression of *RORA* and validated targets in the human brain.

Methods: Functional knockdown of hormone receptors and coregulators with small interfering RNA (siRNA) was used to investigate their involvement in sex hormone regulation of *RORA* in human neuronal cells. DNA methylation analysis is being used to analyze hormone-induced epigenetic changes at the *RORA* promoter. ChIP-on-chip analysis was used for genome-wide identification of putative transcriptional targets of RORA, followed by validation of selected targets by *RORA* knockdown and ChIP-qPCR analyses. Expression of validated targets was also examined in RORA-deficient brain tissues from individuals with ASD. Gene expression data from the BrainSpan human brain atlas is being examined to determine the relative expression of *RORA* and validated target genes in brain tissues from normal males and females.

Results: AR and its corepressor SUMO1 are involved in the suppression *RORA* expression by androgen, while ERα and coactivator NCOA5 collaborate in the up-regulation of *RORA* by estrogen. Over 2500 genes were identified as putative targets of RORA, of which more than 400 are listed in autism gene databases. Gene ontology analysis of this dataset of genes reveals statistically significant enrichment in biological functions negatively impacted in individuals with ASD, including neuronal differentiation, adhesion, synaptogenesis, synaptic transmission/plasticity, and axonogenesis, as well as higher level functions such as cognition, memory, and spatial learning. Six validated targets of RORA were also found to be reduced in RORA-deficient postmortem cortical tissues from individuals with ASD. Epigenetic analyses and the meta-analysis of gene expression in brain are still in progress.

Conclusions: Deficiency of RORA causes dysregulation of multiple neurologically-relevant genes, thus compromising their associated pathways and functions which, in turn, may contribute to the underlying pathobiology of ASD. Differential recruitment of corepressor and coactivator proteins to the *RORA* promoter by the androgen and estrogen receptors, respectively, not only explains the opposite regulation by male and female hormones, but also reveals another layer of complexity in gene regulation in ASD. Moreover, the specific coregulators recruited by the hormone receptors are expected to lead to epigenetic changes that suppress or activate *RORA* expression in response to androgen and estrogen.

**183.003** Multimodal Developmental Neuroimaging of Girls with Autism. K. A. Pelphrey*, A. Jack, L. C. Anderson, D. Z. Bolling, R. J. Jou, D. Yang and B. C. Vander Wyk, *Yale University*

Background: Autism Spectrum Disorder (ASD) disproportionately affects ♂ relative to ♀. Clear explanations for this bias have not emerged because of inconsistent and incomplete phenotyping and small sample sizes. Girls and boys with ASD may well differ in terms of etiological pathways, developmental profiles, symptom expression, and response to treatment.

Objectives: Using structural magnetic resonance imaging (sMRI), functional MRI (fMRI), diffusion tensor imaging (DTI), and electroencephalography (EEG), we are identifying sex differences in brain structure, function, connectivity, and temporal dynamics in ASD.

Methods: We will present the results from two data sets to illustrate some of the earliest findings from this ongoing, five-year study. First, using sMRI at 3 Tesla, we performed *in vivo* evaluation and comparison of cortical thickness among 209, 4- to 12-year-old children with ASD (*n*=25♀,75♂) and age- and IQ-matched typically developing children (TD, *n*=28♀,42♂), and unaffected siblings (US, *n*=17♀,22♂). We evaluated sex differences in: a) state regions, where the cortical thickness in ASD was thinner than TD and US; b) trait regions, where cortical thickness in TD children was thicker than ASD and US; and c) compensatory regions, where cortical thickness in US was thicker than both ASD and TD. Second, using fMRI and a task involving the visual perception of point-light displays (PLDs) of coherent and scrambled biological motion, we discovered sex differences in the normative development of neural systems for social perception in a sample of 38 (19♀) TD children and adolescents (9–14 years old).

Results: Regarding sMRI, state and compensatory regions were localized mainly to the temporal and frontal lobes as well as the insular cortex. Among the state regions, the cortical thickness of the right posterior superior temporal sulcus (pSTS) and that of the right lateral orbitofrontal cortex were negatively correlated with ADOS module 3 social affect scores ($p < .01$, corrected), suggesting that cortical thickness in these regions is a sensitive biomarker of social dysfunction in ASD. Sex differences consisted of a trend toward ♀ US exhibiting increased cortical thickness in the compensatory regions relative to ♂ US. Regarding the fMRI data, we conducted a voxel-wise Sex (male, female) x Condition (biological, scrambled) ANOVA to identify sex differences in the brain response to biological versus scrambled motion ($p< 0.01$, k =21, whole-brain corrected). ♀ relative to ♂ TD children and adolescents exhibited an enhanced response to biological > scrambled motion in the amygdala and ventromedial prefrontal cortex (vmPFC). Psychophysiological interactions analyses revealed increased functional connectivity among the vmPFC, amygdala, and pSTS in ♀ relative to ♂ TD children and adolescents.

Conclusions: With the sMRI dataset, we generally replicated our prior fMRI findings (Kaiser et al., 2010, *PNAS*), while identifying additional state and compensatory regions and providing initial evidence for sex differences in cortical thickness in boys and girls with ASD. Our fMRI findings suggest that the robust, potentially protective, neural circuitry supporting social perception in TD ♀, which normally diverges from males in early adulthood, may underlie a sex bias in ASD.

**183.004** Measuring "Camouflage" in Males and Females with Autism: Clinical, Cognitive, and Neuroanatomical Associations. M. C. Lai*[1], M. V. Lombardo[2], A. N. Ruigrok[1], J. Suckling[1], B. Chakrabarti[1], B. Auyeung[1], C. Ecker[3], M. C. Craig[3], D. G. Murphy[3], E. Bullmore[1], M. AIMS Consortium[4] and S. Baron-Cohen[1], (1)*University of Cambridge*, (2)*University of Cyprus*, (3)*Institute of Psychiatry, King's College London*, (4)*Institute of Psychiatry, King's College London; Autism Research Centre, University of Cambridge; Autism Research Group, University of Oxford*

Background: Clinicians have observed that some high-functioning adults with autism, particularly females, 'camouflage' their social-communication difficulties, often leading to anxiety and/or depression. This phenomenon has not yet been measured, and its cognitive-biological bases remain unclear.

Objectives: To (1) quantify 'developmental change' (DC) and 'camouflage' (CF) in high-functioning adults with autism and compare that between males and females; (2) test the hypotheses that higher CF is associated with more severe anxiety/depression, and cognitively better signal detection from background events and more conservative responses; and (3) explore the neuroanatomical bases of CF.

Methods: Data from age- and IQ-matched high-functioning adult males and females with autism (N=30/group) were analyzed. Childhood ADI-R and current ADOS social-communication, Autism Spectrum Quotient (AQ), and 'Reading the Mind in the Eyes' Task (RMET) scores were all standardized (mean-centered and uniformly scaled [divided by maximum possible score of each]). DC was operationalized as the difference between ADI-R and ADOS ($S_{ADI\text{-}R} - S_{ADOS}$, higher scores reflect more 'decline' in autistic features). 'Camouflage' was operationalized as the

discrepancy between internal 'actual' states and external behavioral presentations in interpersonal contexts, quantified as the difference between self-report autistic traits and explicit behaviors ($S_{AQ}-S_{ADOS}$), and between mentalizing ability and explicit behaviors ($-S_{RMET}-S_{ADOS}$). Their first principle component score was taken as a parsimonious CF measure (higher scores reflect more 'masking'). Depression/anxiety were measured by the Beck Depression/Anxiety Inventories (BDI/BAI). Signal-sensitivity and response bias were measured using a Go/No-Go task. Non-linearly normalized gray and white matter segments estimated from structural MRI (3T-system) were used for behavior-neuroanatomy analyses by mass-univariate general linear models and multivariate pattern recognition approach (Gaussian process regression, leave-one-out-cross-validation, 5000 permutations assessing significance).

Results: Both DC and CF were normally distributed and unrelated to age or IQ. Females scored significantly higher than males (DC: $p$=.030; CF: $p$<.001). CF was positively correlated with BDI (but not BAI) (Pearson's $r$=.301, $p$=.019) and Go/No-Go sensitivity (but not response bias) ($r$=.311, $p$=.017). However when sex-stratified, the CF-BDI correlation was significant in males ($r$=.533, $p$=.002) but not females ($r$=.030, $p$=.876), and the CF-sensitivity correlation was significant in females ($r$=.432, $p$=.017) but not males ($r$=.233, $p$=.223); sex differences in correlations (testing the significance of CF-by-sex interactions) were both at trend-level ($p$=.068, $p$=.072). In the whole sample CF was negatively correlated with gray matter volume at right middle superior temporal gyrus and rolandic operculum, and correlations were sex-dependent at left medial temporal lobe and cerebellum (males: positive; females: negative) and left dorsolateral prefrontal cortex (males: negative; females: non-significant). Total gray matter voxels had modest predictive power for CF in males (correlation=.27, $p$=.029; mean-squared-error=.14, $p$=.030) but not in females; white matter had no predictive power.

Conclusions: On average, high-functioning adult females with autism showed more 'camouflage' than high-functioning adult males with autism, with substantial variability in both sexes. Higher camouflage was associated with more depressive symptoms in males, and better signal-detection sensitivity in females. The neuroanatomical associations of camouflage were partly sex-dependent. The measurement, mechanisms, consequences, and heterogeneity of 'camouflage' in autism warrant further investigation.

### 184 Annual Business Meeting

INSAR Annual Business Meeting - All INSAR members are invited. President and Committee Reports are presented to update members on Society news.